

THE FACTS ON FILE ENCYCLOPEDIA OF
HEALTH AND MEDICINE
IN FOUR VOLUMES:
VOLUME 3

An Amaranth Book

To your health!

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The Facts On File Encyclopedia of Health and Medicine in Four Volumes: Volume 3

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FOREWORD

A big part of my role as a physician is educating my patients about their health. I take as much time as each person needs to explain prevention measures, test results, and treatment options. I encourage questions. But in the moment, sitting there in my office, most people do not yet know what to ask me. By the time questions flood their thoughts, they may be back at work or at home.

Numerous events and circumstances can challenge health, and we all need to know what actions we can take to keep ourselves healthy as well as to obtain appropriate treatment for health conditions that do affect us. Knowledge empowers all of us to make informed and appropriate decisions about health care. Certainly there is no shortage of reference material. Yet there is *so* much information available today! Even for physicians, it is challenging to keep up. How can you get to the core of what you want to know, reliably and to the level of detail you need?

The Facts On File Encyclopedia of Health and Medicine is a great resource for up-to-date health information presented in a manner that is both comprehensive and easy to understand no matter what your level of medical knowledge. The encyclopedia organizes entries by body system. The progression of body systems—and entries—throughout the encyclopedia presents topics the way you think about them.

Going beyond this basic structure, however, is another layer of organization that particularly appeals to me, which is a comprehensive structure of cross references that integrates entries across body systems. After all, your body functions in an integrated way; so, too, should a reference series that discusses your body's health. Not very much that happens with your health affects one part of

your body in isolation from other body structures and functions. Your body attempts to compensate and adjust, often without your awareness, until it can no longer accommodate the injury or illness. The symptoms you bring to your doctor may reflect this compensation, for example frequent headaches that point not to brain tumor (as many people fear but is very rare) but to eye strain or muscle tension or sometimes to hypertension (high blood pressure).

In my medical practice I emphasize integrative health care, embracing the philosophy that health exists as the intricate intertwining of the body's many systems, structures, and functions. So, too, does the care of health. I received my medical degree from Tufts University School of Medicine in Boston, an institution noted for remaining at the forefront of the medical profession. I also completed clinical programs in Mind-Body Medicine at Harvard University, Integrative Medicine at the University of Arizona School of Medicine, and Medical Acupuncture at the University of California-Los Angeles (UCLA). I am a board-certified obstetrician-gynecologist, a board-certified clinical nutritionist, and a licensed acupuncturist. I see patients in my practice in Cincinnati, Ohio; I teach, I lecture, and I frequently go on television and radio to talk about health topics. In each of these areas, I encourage people to think about their health and health concerns from an integrative perspective. When you understand your health from multiple dimensions, you can better understand what to do to keep yourself as healthy as possible.

I wish you the best of health for all of a long, satisfying life. But when the time comes that you must make decisions about medical care, I want you to have the knowledge to make informed

choices that are right for you. Whether you start here and move on to more specialized resources or locate all the information you need within these four volumes, you will find *The Facts On File*

Encyclopedia of Health and Medicine to be a most valuable reference resource.

—**Maureen M. Pelletier, M.D., C.C.N.,
F.A.C.O.G.**

HOW TO USE

THE FACTS ON FILE ENCYCLOPEDIA OF HEALTH AND MEDICINE

Welcome to *The Facts On File Encyclopedia of Health and Medicine*, a four-volume reference set. This comprehensive resource is an indispensable reference for students, allied health professionals, physicians, caregivers, lay researchers, and people seeking information about health circumstances and conditions for themselves or others. Entries present the latest health concepts and medical knowledge in a clear, concise format. Readers may easily accumulate information and build a complete medical profile on just about any health or medical topic of interest or concern.

A New Paradigm for the Health and Medical Encyclopedia

As the art and science of health and medicine continues to evolve, with complex and elegant discoveries and new techniques, medications, and treatments emerging all the time, the need has arisen for a new paradigm for the encyclopedia of health and medicine—a rethinking of the old, and increasingly outmoded, presentations. Carefully researched and compiled, *The Facts On File Encyclopedia of Health and Medicine* offers many distinguishing features that present readers and researchers with an organization as up-to-date and compelling as the breakthrough information its entries contain.

Recognizing the current emphasis on presenting a truly integrative approach to both health and disease, *The Facts On File Encyclopedia of Health and Medicine* organizes content across volumes within a distinctive format that groups related entries by body system (for example, “The Cardiovascular System”) or by general health topic (for example, “Genetics and Molecular Medicine”):

- **Volume 1** presents the sensory and structural body systems that allow the body to engage

with its surroundings and the external environment.

- **Volume 2** presents the cell- and fluid-based body systems that transport nutrients, remove molecular wastes, and provide protection from infection.
- **Volume 3** presents the biochemical body systems that support cellular functions.
- **Volume 4** presents topics that apply across body systems (such as “Fitness: Exercise and Health”) or that address broad areas within health care (such as “Preventive Medicine”).
- The appendixes provide supportive or additional reference information (such as “Appendix X: Immunization and Routine Examination Schedules”).

Following Research Pathways

The Facts On File Encyclopedia of Health and Medicine’s organization and structure support the reader’s and researcher’s ease of use. Many encyclopedia users will find all the information they desire within one volume. Others may use several or all four of the encyclopedia’s volumes to arrive at a comprehensive, multifaceted, in-depth understanding of related health and medical concepts and information. Researchers efficiently look up information in *The Facts On File Encyclopedia of Health and Medicine* in several ways.

Each section’s entries appear in alphabetical order (except the entries in Volume 4’s “Emergency and First Aid” section, which are grouped by type of emergency). The researcher finds a desired entry by looking in the relevant volume and section. For example, the entry for **acne** is in Volume 1 in the section “The Integumentary System” and the entry for **stomach** is in Volume 3 in

the section “The Gastrointestinal System.” The researcher can also consult the index at the back of the volume to locate the entry, then turn to the appropriate page in the volume.

Terms that appear in SMALL CAPS within the text of an entry are themselves entries elsewhere in *The Facts On File Encyclopedia of Health and Medicine*. Encyclopedia users can look up the entries for those terms as well, for further information of potential interest. Such SMALL CAPS cross references typically provide related content that expands upon the primary topic, sometimes leading the user in new research directions he or she might otherwise not have explored.

For example, the entry **hypertension** is in the section “The Cardiovascular System.” The entry presents a comprehensive discussion of the health condition hypertension (high blood pressure), covering symptoms, diagnosis, treatment options, risk factors, and prevention efforts. Among the numerous SMALL CAPS cross references within the hypertension entry are the entries for

- **retinopathy**, an entry in the section “The Eyes” in Volume 1, which discusses damage to the eye that may result from untreated or poorly managed hypertension
- **blood pressure**, an entry in the Volume 2 section “The Cardiovascular System,” which discusses the body’s mechanisms for maintaining appropriate pressure within the circulatory system
- **stroke** and **heart attack**, entries in Volume 2’s “The Cardiovascular System” about significant health conditions that may result from hypertension
- **kidney**, an entry in the section “The Urinary System” in Volume 3, which discusses the kidney’s role in regulating the body’s electrolyte balances and fluid volume to control blood pressure
- **atherosclerosis**, **diabetes**, **hyperlipidemia**, and **obesity**, entries in the sections “The Cardiovascular System” in Volume 2, “The Endocrine System” in Volume 3, and “Lifestyle Variables: Smoking and Obesity” in Volume 4, and all of which are health conditions that contribute to hypertension

Following the path of an encyclopedic entry’s internal cross references, as shown above, can illuminate connections between body systems; define and apply medical terminology; reveal a broad matrix of related health conditions, issues, and concerns; and more. The SMALL CAPS cross references indicated within the text of encyclopedic entries lead encyclopedia users on wide-ranging research pathways that branch and blossom.

At the end of the entry for **hypertension** a list of cross references gathered in alphabetical order links together groups of related entries in other sections and volumes, such as **smoking cessation** in Volume 4’s “Lifestyle Variables: Smoking and Obesity,” to provide specific, highly relevant research strings. These *see also* cross references also appear in SMALL CAPS, identifying them at a glance. Encyclopedia users are encouraged to look here for leads on honing research with precision to a direct pathway of connected entries.

So, extensive cross-references in *The Facts On File Encyclopedia of Health and Medicine* link related topics within and across sections and volumes, in both broad and narrow research pathways. This approach encourages researchers to investigate beyond the conventional level and focus of information, providing logical direction to relevant subjects. Each cross-referenced entry correspondingly has its own set of cross references, ever widening the web of knowledge.

Using the Facts On File Encyclopedia of Health and Medicine

Each section of the encyclopedia begins with an overview that introduces the section and its key concepts, connecting information to present a comprehensive view of the relevant system of the human body or health and medical subject area. For most body systems, this overview begins with a list and drawings of the system’s structures and incorporates discussion of historic, current, and future contexts.

Entries present a spectrum of information from lifestyle factors and complementary methods to the most current technologic advances and approaches, as appropriate. Text that is set apart or bold within an entry gives an important health warning, or targets salient points of interest to add layers of meaning and context. Lists and tables

collect concise presentations of related information for easy reference.

Each type of entry (mid-length and longer) incorporates consistent elements, identified by standardized subheadings:

- **Entries for health conditions and diseases** begin with a general discussion of the condition and its known or possible causes and then incorporate content under the subheadings “Symptoms and Diagnostic Path,” “Treatment Options and Outlook,” and “Risk Factors and Preventive Measures.”
- **Entries for surgery operations** begin with a general discussion of the procedure and then incorporate content under the subheadings “Surgical Procedure,” “Risks and Complications,” and “Outlook and Lifestyle Modifications.”
- **Entries for medication classifications** begin with a general discussion of the type of medication and its common uses and then incorporate content under the subheadings “How These Medications Work,” “Therapeutic Applications,” and “Risks and Side Effects.”
- **Entries for diagnostic procedures** begin with a general discussion of the test or procedure and then incorporate content under the subheadings “Reasons for Doing This Test,” “Preparation, Procedure, and Recovery,” and “Risks and Complications.”

Entries in Volume 4’s section “Emergency and First Aid” are unique within the orientation of *The Facts On File Encyclopedia of Health and Medicine* in that they feature instructional rather than informational content. **These entries do not replace appropriate training in emergency response and first aid methods.** Rather, these entries provide brief directives that are appropriate for guiding the actions of a person with little or no first aid training who is first on the scene of an emergency.

Each volume concludes with a complete, full index for the sections and entries within the volume. Volume 4 of *The Facts On File Encyclopedia of Medicine* contains a comprehensive index for all four encyclopedia volumes that researchers can use to quickly and easily determine which volumes contain desired sections or entries.

The Facts On File Encyclopedia of Health and Medicine in Four Volumes

Volume 1

The Ear, Nose, Mouth, and Throat
The Eyes
The Integumentary System
The Nervous System
The Musculoskeletal System
Pain and Pain Management
Volume Index

Volume 2

The Cardiovascular System
The Blood and Lymph
The Pulmonary System
The Immune System and Allergies
Infectious Diseases
Cancer
Volume Index

Volume 3

The Gastrointestinal System
The Endocrine System
The Urinary System
The Reproductive System
Psychiatric Disorders and Psychologic Conditions
Volume Index

Volume 4

Preventive Medicine
Alternative and Complementary Approaches
Genetics and Molecular Medicine
Drugs
Nutrition and Diet
Fitness: Exercise and Health
Human Relations
Surgery
Lifestyle Variables: Smoking and Obesity
Substance Abuse
Emergency and First Aid
Appendixes:
 I. Vital Signs
 II. Advance Directives
 III. Glossary of Medical Terms
 IV. Abbreviations and Symbols
 V. Medical Specialties and Allied Health Fields
 VI. Resources
 VII. Biographies of Notable Personalities
 VIII. Diagnostic Imaging Procedures
 IX. Family Medical Tree
 X. Immunization and Routine Examination
 Schedules
 XI. Modern Medicine Timeline
 XII. Nobel Laureates in Physiology or Medicine
Selected Bibliography and Further Reading
Series Index: Volumes 1–4

PREFACE TO VOLUME 3

Volume 3 of the four-volume *The Facts On File Encyclopedia of Health and Medicine* presents the body systems that support the body through biochemical functions. From the breakdown of foods into nutrient forms the body can use to the intertwining of hormones with nearly every other body system, biochemistry is the basis of cellular function.

The Gastrointestinal System

Leading Volume 3 is “The Gastrointestinal System,” presenting the organs, structures, and functions that deliver nutrients to cells throughout the body. Complex biochemical processes break down all consumed foods into their basic molecular structures, the biochemical forms the body’s cells can use.

No matter what a food’s original form—apple, steak, french fries—the gastrointestinal system reduces it to molecules. The body then uses the molecules for fuel to maintain cellular activity and metabolism. Among the nutrients essential to sustain life are vitamins, minerals, carbohydrates, proteins, and fats.

As efficient as these processes are for distilling foods into nutrients, there is of course material the body cannot digest or use. The gastrointestinal system takes care of that, too, carrying solid waste from the body.

The Endocrine System

The endocrine system is the body’s network of glands and hormones. Glands produce hormones, the chemical messengers that direct myriad activities within the body. The hormones the endocrine system produces interact with every other body system and are responsible for key functions such as metabolic rate, blood pressure, and the sleep-wake (circadian) cycle.

Hormones also manage the processes of digestion. Fat molecules (lipids) are essential for the production of many hormones. Estrogen brings the process full circle through its role in how the body breaks down and uses lipids.

The most common association many people have with hormones is their role to regulate growth and to initiate and maintain secondary sexual characteristics and reproductive ability. Following a person’s unique genetic blueprint, hormones determine how fast and how tall the person grows. Hormones also give a man his deep voice and regulate a woman’s menstrual cycle.

The Urinary System

The urinary system contains the organs and structures that filter biochemical wastes from the blood and excrete them from the body. All blood passes through the kidneys, which filter from it the wastes of cellular metabolism. If allowed to accumulate in the blood circulation, these wastes rapidly become toxic. Through their filtration functions, the kidneys also maintain the body’s fluid and electrolyte levels to help regulate blood pressure. These versatile organs also produce hormones essential for blood pressure regulation.

The kidney was the first organ to be successfully transplanted, and today kidney transplantation is the most commonly performed transplant operation. Thousands of people receive transplanted kidneys every year in the United States; kidney transplantation is the only successful treatment for end stage renal disease, a common complication of diabetes and hypertension (high blood pressure).

Some structures of the male urinary system—the penis, urethra, and prostate gland—do double duty as organs of the male reproductive system.

The Reproductive System

The organs, structures, and functions of the reproductive system make possible the continuation of human life. The reproductive system remains in a state of immaturity until puberty, when the endocrine system initiates hormonal changes to stimulate the development of secondary sexual characteristics. Hormones remain the foundation of reproductive function for all of adulthood.

Pregnancy, the key function associated with the reproductive system, represents an intricate physiologic choreography in which female and male gametes—ovum and sperm—unite to establish a new life. The woman's body carries the new life for nearly 10 months, changing and adapting, as a result of hormones, until it is capable of independent survival.

Psychiatric Disorders and Psychologic Conditions

Biochemical balance and imbalance are integral to the functions and conditions that involve the mind and emotions. The section "Psychiatric Disorders and Psychologic Conditions" brings Volume 3 to a close. Though much of the working of the mind remains a mystery, researchers have made much progress to understand the integrated functions of the endocrine and nervous systems as they relate to psychiatric disorders and psychologic conditions.

Pharmaceutical therapies (medications) to alter neurotransmitter balances in the brain are often the foundation of treatment approaches. Their effects on neurologic function and emotional processes can be profound, even when doctors do not entirely understand the mechanisms of action that produce such results.

THE FACTS ON FILE ENCYCLOPEDIA OF

HEALTH AND MEDICINE

IN FOUR VOLUMES:

VOLUME 3

THE GASTROINTESTINAL SYSTEM

The gastrointestinal system converts ingested foods to nutrients the body can absorb and use. Physician specialists who treat gastrointestinal conditions are gastroenterologists. This section, “The Gastrointestinal System,” presents a discussion of gastrointestinal structures and their functions, an overview of gastrointestinal health and disorders, and entries about the health conditions that can affect the gastrointestinal system.

Structures of the Gastrointestinal System

MOUTH	cystic duct
hard palate	hepatic duct
soft palate	PANCREAS
cheeks	pancreatic duct
SALIVARY GLANDS	accessory pancreatic duct
TEETH	SMALL INTESTINE
tongue	DUODENUM
lips	ampulla of Vater
epiglottis	ILEUM
ESOPHAGUS	JEJUNUM
lower esophageal sphincter	COLON
stomach	APPENDIX
fundus	CECUM
rugae	ascending colon
gastric glands	transverse colon
pylorus	descending colon
pyloric sphincter	sigmoid colon
LIVER	RECTUM
GALLBLADDER	ANUS
common bile duct	

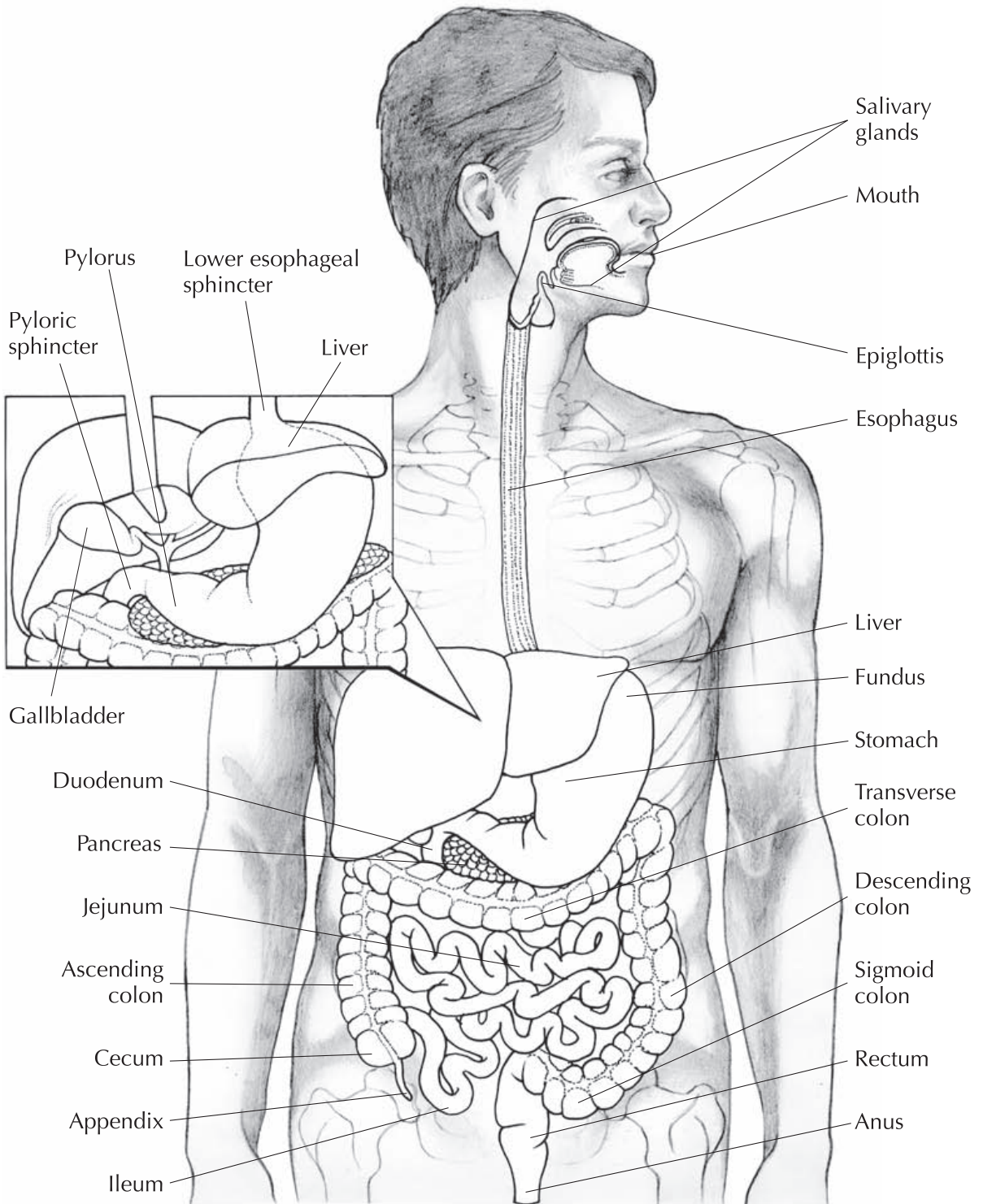
Functions of the Gastrointestinal System

TRADITIONAL CHINESE MEDICINE (TCM), a centuries-old philosophy of health centered on balance among the body’s systems and functions, views the torso as the “triple burner” or “triple heater.” Here the upper, middle, and lower segments of the body converge, becoming the core that distributes energy throughout the body much like a burner or heater. Western medicine shares a similar understanding, translated into the tangibility of physical structures and their functions.

The gastrointestinal system, also called the digestive or alimentary system, functions as the body’s furnace. Fuel—food—enters the gastrointestinal tract in raw form at the MOUTH. Some 20 hours or so later, the compressed residue—feces, also called stool—exits at the other end of the gastrointestinal tract, from the ANUS. Along its passage, the food undergoes numerous transformations as the gastrointestinal organs and structures break it down, mechanically and chemically, into particles and eventually into molecules of energy (NUTRIENTS) that the bloodstream can transport to cells throughout the body. That the typical adult eats three to five times (or more) in 24 hours, yet the body often passes a single BOWEL MOVEMENT in the same period is testament to the gastrointestinal system’s efficiency in extracting every molecule, literally, of useful matter from all that food.

The LIVER and PANCREAS produce numerous chemical substances to aid in breaking down the core nutrients of food—carbohydrate, protein, and fat—into molecules that can pass through the membrane of the small intestine to enter the bloodstream. The liver synthesizes BILE, a complex fluid containing water, electrolytes, cholesterol, biliary acids, and BILIRUBIN (400 to 800 milliliters per day). A network of channels, the BILE DUCTS, collect bile from the liver and transport it to the GALLBLADDER. The gallbladder extracts water from the bile to form a concentrated solution, which it stores until DIGESTIVE HORMONES signal the need to release bile for digestion. The bile flows through another duct, the common bile duct, mixes with

The Gastrointestinal System



pancreatic juices, and drains into the DUODENUM, the first part of the SMALL INTESTINE. INSULIN is the best known of the pancreatic products, though the pancreas synthesizes a number of other important hormones, DIGESTIVE ENZYMES, and juices essential for digestion. Digestive hormones orchestrate and synchronize the multitude of gastrointestinal functions.

Mechanical preparation: the mouth The digestive journey begins with the mouth. Each mouthful of food passes between the crushing force of the TEETH, which can exert up to 3,500 pounds per square inch, at least two dozen times. The taste, texture, and smell of the food induce the SALIVARY GLANDS to release saliva, a watery liquid that contains the digestive enzyme amylase. Amylase begins to break down carbohydrates in the food into the sugar molecules that form them, getting a head start on extracting from food the body's most significant fuel source. The lips and cheeks hold the food in the mouth while the tongue pushes the food under the teeth and against the palate (roof of the mouth). These actions grind the food and mix the particles with saliva to form a paste-like wad called a bolus. Finally the tongue pushes the bolus to the back of the THROAT for swallowing. A small projection of cartilaginous tissue that hangs at the back of the throat, the epiglottis, closes across the TRACHEA (windpipe) to direct the bolus of food down the ESOPHAGUS.

Wavelike contractions—PERISTALSIS—propel the bolus down the esophagus, a muscular tube about 12 inches long. The MUSCLE structure of the esophagus changes along its length, transitioning from striated muscle tissue that responds to voluntary control to smooth muscle tissue, completely under direction of the autonomic NERVOUS SYSTEM. Esophageal peristalsis thrusts the swallowed food bolus toward the STOMACH with such vigor that the food continues to its destination even if the person is upside down. A ring of muscle, the lower esophageal sphincter, opens to pass the bolus into the stomach then closes to keep it there.

Liquefaction: the stomach The pouchlike stomach can expand to five or six times its empty size to accommodate the meals that come its way. This is where the process of digestion gets under way; the stomach digests more than half the carbohydrates and about 20 percent of the protein that a meal

contains. The stomach resides below the DIAPHRAGM, its upper portion resting under the apex of the HEART and near the SPLEEN, just under the left ribs, and its lower portion beneath the liver.

The inside of the stomach is the gastric mucosa, a thick layer of mucous membrane. A network of deep folds, called rugae, gives the gastric mucosa a furrowed appearance. At the bottom of the folds of the rugae are the gastric glands, which produce hydrochloric acid and digestive enzymes (gastric juices). Near the top of the folds are the cells that produce the mucus that protects the stomach's lining from the gastric juices. When the stomach expands with food the rugae flatten, spreading the mucus and expanding the surface area of the stomach for thorough mixing of food with gastric juices. The gastric mucosa also secretes the digestive hormone gastrin.

Three layers of muscle give the stomach STRENGTH and FLEXIBILITY. The innermost layer wraps obliquely, or diagonally, around the gastric mucosa. The middle layer encircles the oblique muscle. The outer layer, the longitudinal muscle, envelopes the stomach lengthwise. Among them, these muscles give the stomach the ability to contract and convolute with considerable force as well as the ability to expand and contract for the volume of food it contains. These layers of muscle also give the stomach the ability to squeeze its contents downward into the small intestine for the rest of the digestive journey.

Food, in a semiliquid state after initial preparation in the mouth, enters at the top of the stomach, called the fundus, and flows downward across the rugae. Gastric juices immediately begin working to dissolve food particles, breaking them down into more basic compounds that the small intestine can digest. At the same time the stomach muscles contract, producing powerful contortions that further mix and liquefy the stomach's contents. The combined chemical and mechanical actions produce chyme, a somewhat soupy solution the stomach then sends to the small intestine. The lower portion of the stomach is the pylorus, from the Greek for "gatekeeper." Chyme exits the stomach through the pyloric sphincter, which relaxes to permit passage into the duodenum. Chyme trickles from the stomach over four to six hours.

4 The Gastrointestinal System

Extracting nutrients: the small intestine The small intestine is where nutrients move from the gut to the blood. The nearly 18 feet of small intestine loop back and forth within the abdominal cavity, framed inside the COLON. Two layers of smooth muscle, the outer longitudinal and the inner circular, form the walls of the small intestine. These muscles rhythmically contract to move digestive matter through the gastrointestinal tract. The intestinal mucosa, a thin mucous membrane, forms the inner lining. It produces a number of digestive enzymes and digestive hormones.

In the first segment of the small intestine, the duodenum, the intestinal mucosa is fairly smooth. Only 10 inches long, the duodenum handles the majority of digestive activity. In addition to receiving chyme from the stomach, the duodenum receives bile and pancreatic juices via the common bile duct, which enters the duodenum at a small port called the ampulla of Vater. These solutions complete the breakdown of foods into end-product nutrients. Bile transforms fats into fatty acids. Pancreatic and intestinal enzymes convert proteins to amino acids and polysaccharides (compound sugars) to monosaccharides (simple sugars). Further chemical interactions separate out vitamins and minerals. Monosaccharides and some electrolytes (salts and minerals) enter the bloodstream through the duodenum, which is also the major site for absorption of iron and calcium.

The watery mixture containing the remaining nutrients moves on to the middle and end segments of the small intestine for absorption. In these segments, the JEJUNUM and the ILEUM, millions of tiny projections called villi extend from the intestinal mucosa to vastly expand the mucosal surface area. A network of capillaries (tiny blood vessels) weaves through the villi. Nutrients pass through the mucosal membrane and into the capillaries, which transport them into the bloodstream and throughout the body. The jejunum, about seven feet long, absorbs the remaining monosaccharides and many amino acids, additional electrolytes, water-soluble vitamins (the B vitamins and vitamin C), folic acid, and minerals such as iron. The final segment of the small intestine, the ileum, is about 10 feet long. It absorbs fatty acids and the remaining amino acids, as well as vitamin B₁₂ and the fat-sol-

uble vitamins (vitamins A, D, E, and K). The ileum also reabsorbs bile salts. The journey through the small intestine takes 8 to 10 hours.

Compacting waste: the colon The colon, also called the large intestine, collects and compacts the remnants of digestion for their elimination from the body, a process it accomplishes primarily by absorbing water. Like the small intestine, the colon's wall contains two layers of muscle, the outer running lengthwise and the inner circling around, that rhythmically contract. The inner lining is flat mucous membrane. The CECUM, the first segment of the colon, is a pouchlike structure that receives digestive material from the ileum, which enters near its floor. The ileocecal valve maintains the passage for one-way movement. The cecum absorbs about a third of the water from the digestive material it receives. Peristalsis then carries the intestinal content from the cecum through the rest of the colon.

The main colon loops around the outer edge of the abdominal cavity. It contains five segments. The ascending colon rises from the cecum and travels up the body's right side. At the gallbladder the colon takes a turn; the next segment is the transverse colon. The transverse colon extends across the top of the abdomen, with the liver and stomach above and the small intestine beneath. It takes a downward turn at the base of the stomach's fundus, becoming the descending colon. The descending colon drops along the left perimeter of the abdominal cavity. The descending colon makes a staggered turn inward toward the midline of the body, becoming the sigmoid colon. These four segments of the colon are functionally contiguous, progressively dehydrating and compacting the digestive residue that moves through them. The final segment of the colon is the RECTUM, by which point digestive waste has reached the solid form known as feces or stool. The rectum stores stool until its expulsion from the body via the anus (bowel movement). The journey through the colon generally takes four to six hours, though can take longer.

Health and Disorders of the Gastrointestinal System

The gastrointestinal system represents an intricate balance of mechanical and chemical functions.

Lifestyle and dietary habits can affect this balance. To help maintain this balance and preserve gastrointestinal health, gastroenterologists recommend

- Eating foods high in fiber such as fruits, vegetables, and whole grains and whole grain products. High-fiber foods move quickly through the gastrointestinal tract and result in residual bulk that helps keep stools soft, reducing the risk for conditions such as CONSTIPATION and HEMORRHOIDS.
- Reducing consumption of foods high in fats. Fats require more steps to digest, slowing movement through the gastrointestinal tract. Saturated (animal) fats are associated with an increased risk for COLORECTAL CANCER.
- Limiting consumption of products that contain CAFFEINE or ALCOHOL, which are frequent causes of DIARRHEA.
- Drinking plenty of noncaffeinated and nonalcoholic fluids throughout the day.
- Chewing food thoroughly before swallowing and remaining upright after eating.

Gastrointestinal symptoms are the second-leading reason for visits to the doctor, with diarrhea being the most common of these symptoms. Many gastrointestinal ailments are minor, such as INFECTION (GASTRITIS, GASTROENTERITIS, and COLITIS) and irritations such as DYSPEPSIA. The close proximity of the lower esophagus and the bottom of the heart gives rise to the term “heartburn,” an apt descriptor for the burning sensation that occurs when gastric contents bubble back up into the esophagus. GASTROESOPHAGEAL REFLUX DISORDER (GERD) develops when such backwash becomes chronic.

Chronic gastrointestinal conditions such as CELIAC DISEASE, DIVERTICULAR DISEASE, IRRITABLE BOWEL SYNDROME (IBS), and INFLAMMATORY BOWEL DISEASE (IBD) can significantly interfere with QUALITY OF LIFE. People who have conditions such as these must work closely with their doctors to develop effective treatment approaches and manage their lifestyles in ways that minimize symptoms and support gastrointestinal health.

Cancers are among the most serious gastrointestinal conditions and can involve any organ or

structure of the gastrointestinal system. Though colorectal cancer remains the second-leading cause of deaths due to cancer in the United States, it also offers great opportunity for prevention as well as early detection and treatment. Doctors now know that detecting and removing intestinal polyps, fleshy growths that develop in the colon’s mucosa, via screening COLONOSCOPY eliminates the foundation for more than 90 percent of colorectal cancers.

HEALTH CONDITIONS OF THE GASTROINTESTINAL SYSTEM

ACHALASIA	ANAL ATRESIA
ANAL FISSURE	APPENDICITIS
BARRETT’S ESOPHAGUS	BEZOAR
BILIARY ATRESIA	BOWEL ATRESIA
CELIAC DISEASE	CIRRHOSIS
COLITIS	COLORECTAL CANCER
CONSTIPATION	Crohn’s disease
CYCLIC VOMITING SYNDROME	DIARRHEA
ESOPHAGEAL ATRESIA	ESOPHAGEAL CANCER
ESOPHAGEAL SPASM	ESOPHAGEAL VARICES
ESOPHAGITIS	FAMILIAL ADENOMATOUS
FECAL IMPACTION	POLYPOSIS (FAP)
FECAL INCONTINENCE	GALLBLADDER DISEASE
GASTRITIS	GASTROENTERITIS
GASTROESOPHAGEAL REFLUX	GASTROINTESTINAL BLEEDING
DISORDER (GERD)	HEMORRHOIDS
GASTROPARESIS	HEPATIC CYST
HEPATIC ABSCESS	HEREDITARY NONPOLYPOSIS
HEPATITIS	COLORECTAL CANCER (HNPCC)
HIATAL HERNIA	ILEUS
HIRSCHSPRUNG’S DISEASE	INFLAMMATORY BOWEL
INTESTINAL ADHESIONS	DISEASE (IBD)
INTESTINAL POLYP	INTUSSUSCEPTION
LIVER CANCER	LIVER DISEASE OF ALCOHOLISM
LIVER FAILURE	MALABSORPTION
PANCREATIC CANCER	PANCREATITIS
PEPTIC ULCER DISEASE	PERITONITIS
PRIMARY BILIARY CIRRHOSIS	PRIMARY SCLEROSING
PROCTITIS	CHOLANGITIS
RAPID GASTRIC EMPTYING	RECTAL FISTULA
RECTAL PROLAPSE	SHORT BOWEL SYNDROME
STEATOHEPATITIS	STOMACH CANCER
TOXIC MEGACOLON	ulcerative colitis
WHIPPLE’S DISEASE	ZOLLINGER-ELLISON SYNDROME

Traditions in Medical History

Ancient doctors learned much about the inner structures and workings of the body from wounds that occurred on the battlefield. The writings of the Roman physician Celsus (14–37 C.E.) documented his recommendations to his students that they take advantage of such natural opportunities. One student who took the advice to heart was GALEN (130–200 C.E.), whose own teachings and writings would shape the understanding and practice of Western medicine for centuries. Galen learned much of the practice of medicine while treating soldiers and gladiators. Of the digestive process, Galen believed stomach liquefied food that then passed to the intestines. From the intestines the mixture traveled to the liver, where it mysteriously became blood that the veins carried around to the various tissues of the body. Though wrong in some fundamental ways, the extrapolation was not so far off from the reality.

In 1822, U.S. Army surgeon William Beaumont became the first physician to witness and explore the functions of the stomach in “real time.” In June of that year French-Canadian trader Alexis St. Martin suffered a musket wound to his left side that opened a fist-size hole in his stomach. St. Martin’s comrades brought him to Beaumont for treatment. Miraculously in an era of no antibiotics and limited surgical expertise, St. Martin survived. With great scientific curiosity, over several decades Beaumont observed the activities of St. Martin’s stomach through this window. He conducted experiments with various items of food tied to string that he periodically withdrew to assess the extent of their demolition in the stomach. He measured the volume and temperature of stomach juices. And he watched the digestive process as much as his schedule and St. Martin’s patience permitted.

Finally, in 1833 Beaumont published his findings in a book, *Experiments and Observations on the Gastric Juice and the Physiology of Digestion*. St. Martin lived 58 years with the hole in his stomach, outliving Beaumont by 27 years and dying at age 86. Beaumont’s detailed observations and experiments gave modern medicine the most extensive understanding of digestion possible until the 1940s when ANESTHESIA and ANTIBIOTIC MEDICATIONS made surgery practical, and surgeons could more

carefully explore the stomach and other gastrointestinal structures.

Breakthrough Research and Treatment Advances

The 21st century arrived on the heels of amazing advances in medical and surgical treatments for gastrointestinal conditions. Among the most significant advances have been those in ORGAN TRANSPLANTATION, which result from a blend of improved surgical techniques, organ harvesting procedures, and immunosuppressive methods. In 1984 LIVER TRANSPLANTATION became the standard treatment for end-stage LIVER FAILURE, a milestone in its progression from experiment to therapeutic solution. Within 15 years surgeons in the United States were performing more than 5,000 liver transplantations a year. Surgeons are now exploring applications for transplantation technology in other conditions, such as to replace the severely diseased small intestine, stomach, and even pancreas. Though these transplant operations remain largely investigational, they hold great promise for people who have disorders such as CYSTIC FIBROSIS, SHORT BOWEL SYNDROME, DIABETES, and severe diverticulosis.

Other advances in diagnostic and operative procedures take advantage of fiberoptic technology. Endoscopic surgery has transformed once-grueling operations, procedures such as open CHOLECYSTECTOMY, which often required up to 12 weeks of recuperation, to a few minor incisions and a third of the recovery time. Surgeons now can perform APPENDECTOMY, herniorrhaphy and hernioplasty, colon resection, and even operations on the stomach with minimally invasive techniques. COLOSTOMY (a surgically created opening through the abdominal wall for the passage of solid digestive waste), once nearly certain after most operations on the colon, now is often temporary or can be avoided altogether. Surgeons have developed methods for anastomosing, or connecting, the remaining segments of the bowel to restore near-normal function. Medications help soothe the bowel and control BACTERIA during HEALING.

The HUMAN GENOME PROJECT, the complete mapping of the human genetic structure, has led to discoveries that have altered the understanding, course of treatment, outlook, and prevention measures for a number of gastrointestinal disor-

ders, including PEPTIC ULCER DISEASE, IBD, and familial cancers of the gastrointestinal tract. GENETIC SCREENING and GENETIC COUNSELING make it possible for people to learn whether they are at risk for many familial or hereditary disorders and take appropriate measures to minimize their likelihood for acquiring the condition. Numerous clinical trials are exploring investigational GENE THERAPY methods to treat or thwart hereditary disorders such as celiac disease and cystic fibrosis.

COLONOSCOPY, visualization of the entire colon using a flexible, lighted endoscope inserted through the anus, has the potential to eliminate 70 percent or more of colorectal cancer through early detection and removal of the adenomatous

polyps that are most often the source of cancerous growths in the colon. Research continues the quest for a less intrusive approach, with the current focus on virtual colonoscopy and other procedures that allow for the visualization of the gastrointestinal tract without entering it (though virtual colonoscopy does not offer the opportunity to remove polyps; conventional colonoscopy remains the therapeutic option of choice for most polypectomies). Researchers are also looking for ways to use ENDOSCOPY to screen for other cancers that often go undetected until they are too advanced for treatment, hoping technology may offer similar preventive benefits for a broader range of gastrointestinal malignancies.



abdominal distention Swelling of the abdomen, sometimes referred to as bloating. Doctors evaluate abdominal distention as a clinical indicator for a wide range of health conditions. The most common cause of transitory abdominal distention is excessive intestinal gas resulting from eating too fast, which results in swallowing of air along with the food. The BACTERIA in the COLON that ferment high-fiber carbohydrates such as vegetables, fruits, and legumes (beans) also produce intestinal gas during digestion. Infants often swallow air when nursing or bottle feeding, which can cause noticeable abdominal distention rather rapidly. “Burping” the infant relieves the distention. Abdominal distention due to EATING HABITS dissipates as the meal moves through the gastrointestinal system. Completely chewing food before swallowing, especially meats and high-fiber foods, helps slow eating, prepare food for digestion, and reduce the amount of air that enters the gastrointestinal system.

Menstruating women often experience transitory abdominal distention in the few days before and during MENSTRUATION, a result of fluid retention related to hormonal changes taking place in the body. Abdominal distention is a normal feature of PREGNANCY. In early pregnancy the distention and corresponding discomforts may mimic gastrointestinal causes, though as the pregnancy continues the characteristic abdominal enlargement becomes apparent. Extreme OBESITY may mask this presentation, however, resulting in the appearance of generalized abdominal distention rather than characteristic pregnancy. Abdominal distention often is an early sign of ECTOPIC PREGNANCY, a life-threatening condition in which the fertilized egg implants in the fallopian tube instead of the UTERUS. Doctors commonly test for preg-

nancy in women of childbearing age who seek treatment for abdominal distention.

Abdominal distention that develops gradually and persists may signal health conditions that require medical attention. The most common cause of prolonged abdominal distention is OBESITY, in which excessive body fat accumulates in the central abdomen. The resulting distention may cause the abdominal wall to protrude or cause generalized thickening through the midsection (the “spare tire” presentation of ABDOMINAL ADIPOSITY). Weight reduction results in the gradual recession of abdominal adiposity. ASCITES is a form of abdominal distention that results from fluid accumulating in the peritoneal cavity. Chronic LIVER disease, HEART FAILURE, and chronic KIDNEY disease are among the health conditions associated with ascites. Less commonly, abdominal distention may signal tumors, UTERINE FIBROIDS, OVARIAN CYST, and other growths affecting the abdominal organs. Abdominal distention is a symptom in numerous gastrointestinal conditions including IRRITABLE BOWEL SYNDROME (IBS), MALABSORPTION disorders, and intestinal obstruction.

The doctor should evaluate abdominal distention that persists or in which there is accompanying PAIN, FEVER, OR GASTROINTESTINAL BLEEDING. Palpation (feeling the abdomen), BARIUM SWALLOW and BARIUM ENEMA, X-ray endoscopic procedures such as gastroscopy and COLONOSCOPY, ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, MAGNETIC RESONANCE IMAGING (MRI), and paracentesis (withdrawing fluid from the abdominal cavity through the abdominal using a needle and syringe) are among the common diagnostic methods the doctor may use to identify the cause of abdominal distention. Treatment targets the underlying conditions.

See also ABDOMINAL PAIN; BODY SHAPE AND CARDIO-VASCULAR DISEASE; [DYSPEPSIA](#); [ENDOSCOPY](#); FALLOPIAN TUBES; [FECAL IMPACTION](#); FLATULENCE; WEIGHT LOSS AND WEIGHT MANAGEMENT.

abdominal pain Discomfort in the trunk region that can range from mild cramping to severe PAIN.

Abdominal pain requires emergency medical attention when:

- **PAIN is sudden, sharp, and unrelenting**
- **Pain radiates into the shoulder or jaw**
- **The abdomen is tense and tender to the touch**
- **There is bloody VOMITING or DIARRHEA**

Abdominal pain is one of the most common reasons people seek medical care. Numerous health conditions can cause abdominal pain, from [DYSPEPSIA](#) (indigestion) and [FLATULENCE](#) (gas) to [APPENDICITIS](#) and [GALLBLADDER DISEASE](#). Advanced or metastatic [CANCER](#), [LIVER](#) disease, and [HEART ATTACK](#) also can involve abdominal pain, among other symptoms.

COMMON CAUSES OF ABDOMINAL PAIN

APPENDICITIS	cholecystitis
cholelithiasis (gallstones)	CONSTIPATION
dissecting abdominal ANEURYSM	DYSPEPSIA (indigestion)
ECTOPIC PREGNANCY	FECAL IMPACTION
GASTROESOPHAGEAL REFLUX DISORDER (GERD)	HEART ATTACK
ILEUS (intestinal obstruction)	HERNIA
NEPHROLITHIASIS (KIDNEY stones)	INTUSSUSCEPTION
PELVIC INFLAMMATORY DISEASE (PID)	PANCREATITIS
URETHRITIS	PERITONITIS
viral GASTROENTERITIS	URINARY TRACT INFECTION
	(UTI)

It is difficult to gauge the severity of the underlying cause of pain on the basis of the pain’s qualities. Intestinal gas can cause immobilizing pain, while heart attack may initially manifest as vague discomfort. [FEVER](#) (body temperature above 100° F) often accompanies bacterial infections, which require treatment with [ANTIBIOTIC MEDICATIONS](#). Most abdominal discomfort is transitory and benign. Abdominal discomfort requires medical attention when pain is debilitating or continues for longer than five days without improvement,

there is discharge from the [PENIS](#) or [VAGINA](#), or there is accompanying [VOMITING](#) or [DIARRHEA](#) for longer than three days.

See also [ABDOMINAL DISTENTION](#).

achalasia A disorder of the [ESOPHAGUS](#) in which the lower esophageal sphincter, the ring of [MUSCLE](#) at the entry to the [STOMACH](#), remains constricted, failing to allow food to pass into the stomach. Researchers believe the cause is a reduced number of inhibitory nerve cells, the specialized neurons that direct involuntary muscle tissue to relax. The resulting imbalance allows excitory [NERVE](#) cells (neurons that direct involuntary [MUSCLE](#) tissue to contract) to dominate. Over time the peristaltic action of the esophagus, a structure of involuntary muscle tissue, slows as well. Symptoms of achalasia include

- painful or difficult swallowing
- regurgitation of swallowed food
- [DYSPEPSIA](#) (heartburn)
- [PAIN](#) in the central chest and beneath the sternum (breastbone) after eating
- unintended weight loss

[BARIUM SWALLOW](#) can suggest the diagnosis, with manometry (which measures the pressure within the esophagus) providing confirmation. The gastroenterologist may also perform esophagogastroduodenoscopy (EGD), an endoscopic examination of the upper gastrointestinal tract, to rule out cancers and to use balloon dilation to gently stretch the sphincter. Some people experience relief with medications, such as calcium channel blockers, which block the actions of excitory neurotransmitters to help relax the lower esophageal sphincter. [BOTULINUM THERAPY](#), in which the gastroenterologist injects botulinum toxin into the sphincter to paralyze it, can provide temporary relief. The treatments of choice for short-term relief are disruption of the lower esophageal sphincter, in which the gastroenterologist uses special instruments to widen the sphincter, or esophagomyotomy, a surgical [OPERATION](#) to cut a portion of the sphincter.

See also [ENDOSCOPY](#); [NERVOUS SYSTEM](#); [NEURON](#); [NEUROTRANSMITTER](#); [PERISTALSIS](#); [SWALLOWING DISORDERS](#).

aging, gastrointestinal changes that occur with

The organs and structures of the gastrointestinal system undergo numerous changes as an individual grows older. At birth, the infant's MOUTH supports sucking and swallowing liquid nourishment. With the eruption of TEETH and the elongation of the head, developmental changes that occur in early childhood, the oral cavity shifts to support chewing and swallowing solid foods. By three years of age most children in the United States are eating fully solid foods, their gastrointestinal systems capable of digesting nearly any food an adult's body can accommodate.

The gastrointestinal system remains fairly stable until about the fourth decade of life, at which time changes in muscle tone, vasculature (blood vessel function and blood supply), and body composition begin to affect its structures and functions. Some of these changes are physiologic and others relate to lifestyle; combined they result in increased gastrointestinal problems such as GASTROESOPHAGEAL REFLUX DISORDER (GERD), GALLBLADDER DISEASE, DIABETES (altered functioning of the PANCREAS), and PEPTIC ULCER DISEASE. Changes such as weight gain or OBESITY may affect digestive functions as well, particularly with ABDOMINAL ADIPOSITY, a pattern of body fat distribution in which excess body fat accumulates in the abdomen. This accumulation can compress the intestines, slowing intestinal motility. In the fifth decade of life and beyond, there is increased risk for STOMACH CANCER, LIVER CANCER, PANCREATIC CANCER, and COLORECTAL CANCER.

Changes in vasculature, which often result from other health circumstances such as HYPERTENSION (high BLOOD PRESSURE) and ATHEROSCLEROSIS, affect gastrointestinal motility and absorption. A person age 50 absorbs about a third less calcium than a person age 25. Absorption of other vital nutrients slows as well; many older adults benefit from NUTRITIONAL SUPPLEMENTS. In the seventh decade of life and beyond, the SALIVARY GLANDS and digestive glands slow production of their respective secretions. Reduced saliva makes chewing and swallowing more difficult; reduced gastric juices further impede digestion and absorption. These changes increase the potential for gastrointestinal disturbances such as DIARRHEA and CONSTIPATION.

Measures to preserve gastrointestinal health can mitigate many of the age-related changes that occur in the gastrointestinal system. These include

- eating a high-fiber, low-fat diet
- drinking six to eight ounces of water every hour or two during waking hours
- maintaining healthy weight
- getting daily physical exercise
- having regular screening, such as COLONOSCOPY, for colorectal cancer
- managing other health conditions such as diabetes

See also GENERATIONAL HEALTH-CARE PERSPECTIVES; HYDRATION; MINERALS AND HEALTH; NUTRITIONAL NEEDS; SIALOADENITIS; SIALORRHEA; VITAMINS AND HEALTH.

anal atresia A CONGENITAL ANOMALY, also called imperforate ANUS, in which the anal opening that allows the elimination of feces is missing or misplaced. Diagnosis typically takes place within 24 to 48 hours following birth, with the passage of, or failure to have, the first BOWEL MOVEMENT. Complete anal atresia requires immediate surgery to create a means for the body to pass stool; often the surgeon creates a temporary COLOSTOMY (opening from the large intestine through the abdominal wall) until the infant can undergo any necessary reconstructive surgery. When partial anal atresia is present, the anus may open into another structure such as the VAGINA or URETHRA. Partial anal atresia also requires surgical repair. After surgical reconstruction of the anus many infants have normal bowel function. However some infants have damage to, or are missing, the nerves that regulate the anal sphincter, with resulting FECAL INCONTINENCE. Anal atresia often occurs in combination with other congenital anomalies, notably NEURAL TUBE DEFECTS.

See also BOWEL ATRESIA; CONGENITAL HEART DISEASE; ESOPHAGEAL ATRESIA; RECTAL FISTULA.

anal fissure Small tears in the tissue around the ANUS. Anal fissures can be internal or external. They typically are painful and may bleed with bowel movements, resulting in small amounts of bright red BLOOD on the toilet tissue or in the toilet bowl.

The most common cause of anal fissure is CONSTIPATION, in which the bowel movement is hard and often forced. PAIN can be intense with bowel movements. The doctor can diagnose anal fissure on the basis of the symptoms and by examining the anal area, though may perform an anoscopy to examine the inner anus. Most anal fissures heal with conservative treatment that includes frequent sitz baths, topical application of hydrocortisone preparations to reduce INFLAMMATION, high-fiber diet and stool softeners to pull more moisture into the stools, and daily physical exercise such as walking to improve intestinal motility (movement of food through the gastrointestinal tract) and encourage regular bowel movements.

The next level of treatment for anal fissure that persists is topical nitroglycerin or topical nifedipine (a calcium channel blocker), both of which increase blood flow to the anal sphincter and cause it to relax. Doctors prescribe these medications in oral form to relax the CORONARY ARTERIES as a treatment for CORONARY ARTERY DISEASE (CAD); the pharmacological action on the blood vessels in the anal area is similar. Nitroglycerin ointment, like other forms of nitroglycerin, can cause HEADACHE and dizziness. Another treatment option is BOTULINUM THERAPY, in which the doctor injects the anal sphincter near the fissure with botulinum toxin to temporarily paralyze the MUSCLE fibers, which relaxes the sphincter. The effect of the botulinum toxin lasts about three months. Extensive anal tears and fissures that do not heal with other treatments may require surgical repair. INFECTION may develop with persistent or extensive anal fissure, and requires appropriate antibiotic therapy.

See also [ENDOSCOPY](#); [HEMORRHOIDS](#); [PROCTITIS](#); [SITZ BATH](#).

antacids Products that neutralize gastric (STOMACH) acid to relieve DYSPEPSIA (heartburn and indigestion). Antacids work by increasing the pH (acid level) of the gastric juices, which reduces the irritation to the stomach tissues. Most antacids contain mineral salts, which are alkaline.

Because of their high salt and mineral content, many antacids can cause CONSTIPATION or DIARRHEA by drawing excessive fluid from the gastrointestinal tract. Sodium bicarbonate, which most people mix at home by dissolving baking soda in water,

has such a high sodium level that it can affect BLOOD PRESSURE and the rhythm of the HEART. Anyone who has CARDIOVASCULAR DISEASE (CVD), especially HYPERTENSION or ARRHYTHMIA, should not use sodium bicarbonate as an antacid.

COMMON ANTACID PRODUCTS	
Active Ingredient	Representative Products
aluminum hydroxide	ALternaGEL
aluminum/magnesium combination	Maalox, Mylanta
bismuth subsalicylate	Pepto-Bismol
calcium carbonate	Tums, Titralac
magnesium hydroxide	milk of magnesia
simethicone	Gas-X, Phazyme
sodium bicarbonate	baking soda

Aluminum hydroxide, though very effective at neutralizing stomach acid, is so likely to cause constipation that it nearly always is combined with magnesium, which has the opposite effect. Doctors may recommend magnesium-based antacids, such as milk of magnesia, as LAXATIVES to treat mild, occasional constipation. Many antacid products also contain simethicone, a surfactant that breaks up intestinal gas bubbles to relieve bloating and FLATULENCE.

Bismuth subsalicylate products such as Pepto-Bismol contain an aspirin-like ingredient that can cause the rare but serious SIDE EFFECT, REYE'S SYNDROME, in children who have viral infections. Children should not take these products.

Antacids are available over the counter, without a doctor's prescription. Occasional use of antacids can provide rapid relief of dyspepsia and other digestive discomforts. Antacids are most effective taken with food, which increases the time the antacid remains in the stomach, and liquid forms seem to be more effective than chewable forms. Chronic or regular use of antacids can result in numerous health problems, ranging from

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“rebound” dyspepsia or gastric reflux (most common with calcium carbonate products) to OSTEO-POROSIS (with magnesium products, as magnesium binds with calcium) and aluminum TOXICITY. Indications of antacid overuse include

- dyspepsia symptoms that seem to surge when the antacid DOSE nears the end of its effectiveness
- the need to take higher or more frequent doses of the antacid to obtain relief
- mental CONFUSION (indicating possible alu-minum toxicity)
- chronic diarrhea (typically with aluminum/magnesium combination products)

Antacids also interfere with the actions of numerous medications. Other products, such as H2 ANTAGONIST (BLOCKER) MEDICATIONS and PROTON PUMP INHIBITOR MEDICATIONS, are more effective for man-aging long-term gastric discomfort such as GAS-

TROESOPHAGEAL REFLUX DISORDER (GERD). Antacids also interfere with H2 antagonist blockers. Chil-dren age 12 and under should not take antacids unless a doctor recommends them. A pharmacist can suggest an appropriate antacid for the circum-stances and to avoid interfering with any medica-tions a person is taking.

See also ANTIDIARRHEAL MEDICATIONS; ANTIEMETIC MEDICATIONS; PEPTIC ULCER DISEASE.

antidiarrheal medications Medications that relieve DIARRHEA. Antidiarrheal medications work by slowing the activity of the gastrointestinal tract or by absorbing more fluid in the COLON (large intestine). Though diarrhea is unpleasant, doctors recommend letting the body restore its balance without medications in most circumstances of acute diarrhea. Acute diarrhea (diarrhea that comes on suddenly) may result from simple gas-trointestinal upset following unusual foods and beverages, (such as when traveling), excessive

COMMON ANTIDIARRHEAL MEDICATIONS		
Active Ingredient	Representative Products	Availability
attapulgite	Kaopectate, Parepectolin	over the counter
belladonna	Donnatal	requires a doctor’s prescription
bismuth subsalicylate	Pepto-Bismol	over the counter
codeine	codeine	requires a doctor’s prescription
difenoxin and atropine	Motofen	requires a doctor’s prescription
diphenoxylate	Lomotil	requires a doctor’s prescription
kaolin and pectin	Kapectolin	over the counter
loperamide	Imodium	over the counter
methylcellulose	Citrucel	over the counter
octreotide	Sandostatin	requires a doctor’s prescription
paregoric	camphorated tincture of opium	requires a doctor’s prescription
psyllium	Metamucil	over the counter

CAFFEINE consumption, FOOD-BORNE ILLNESSES, or viral INFECTION (GASTROENTERITIS or ENTERITIS). These circumstances tend to resolve themselves within a few days, which may be briefer than the actions of many antidiarrheal medications.

Taking an antidiarrheal product may result in rebound CONSTIPATION. However, diarrhea more significantly interferes with daily activities than does constipation, and many people opt to take medications to slow or stop it. It is important to drink extra fluids when taking antidiarrheal medications, to replace fluids lost with the diarrhea as well as to maintain adequate hydration of the gastrointestinal tract to prevent rebound constipation from developing. Some antidiarrheal medications are available over the counter and others require a doctor's prescription.

Doctors sometimes prescribe anticholinergic medications, which act on the NERVOUS SYSTEM to slow gastrointestinal function, for severe diarrhea. However, these medications have numerous actions throughout the body, and doctors tend to reserve them for use when other antidiarrheal medications are ineffective. Opiate NARCOTICS such as paregoric and codeine are effective for slowing gastrointestinal motility. Attapulgit, pectin, and kaolin are natural substances that absorb fluid. Though typically perceived as LAXATIVES, bulking agents such as psyllium and methylcellulose also absorb water and can help restore normal bowel function.

Antidiarrheal medications are most effective for controlling outbreaks of diarrhea such as may occur with IRRITABLE BOWEL SYNDROME (IBS), INFLAMMATORY BOWEL DISEASE (IBD), and MALABSORPTION. Antidiarrheal medications are also effective for treating antibiotic-induced diarrhea that does not end when the antibiotic therapy ends. Remedies such as taking lactobacillus or eating plain yogurt may help restore normal BACTERIA to the gastrointestinal tract.

The most frequent complication of antidiarrheal medications is rebound constipation. A rare but serious complication that can occur when taking antidiarrheal medications that slow gastrointestinal motility is TOXIC MEGACOLON, in which the colon becomes vastly dilated and flaccid and the flow of the intestinal content stops. Antidiarrheal medications also can mask conditions that require

medical attention. For most people, occasional use of over-the-counter antidiarrheal medications provides prompt relief of diarrhea with few complications.

See also [ANTACIDS](#); ANTIEMETIC MEDICATIONS; [FIBER AND GASTROINTESTINAL HEALTH](#).

antiemetic medications Medications that relieve NAUSEA and VOMITING (known clinically as emesis). The most commonly used are anticholinergic medications and antihistamine MEDICATIONS, which suppress the vestibular system mechanisms that cause vomiting. Many antihistamine products are available over the counter. Doctors may recommend or prescribe these medications to treat nausea related to VERTIGO, MÉNIÈRE'S DISEASE, LABYRINTHITIS, and other disorders of the inner EAR and vestibular system, and to help prevent motion sickness. Both anticholinergics and antihistamines can cause drowsiness and dry MOUTH.

A classification of powerful antiemetics, the 5-HT₃ RECEPTOR ANTAGONIST MEDICATIONS, became available in the 1990s. Doctors prescribe these medications, such as dolasetron and ondansetron, primarily to treat nausea and vomiting resulting from RADIATION THERAPY, CHEMOTHERAPY, and surgery. These medications work by blocking serotonin from reaching receptors in the gastrointestinal system and may have neurologic side effects such as Parkinson-like symptoms.

Over-the-counter products to treat nausea include bismuth subsalicylate (Pepto-Bismol) and cola syrup, both of which are effective for relieving mild nausea and vomiting with viral INFECTION (such as GASTRITIS and GASTROENTERITIS). Pharmacies also sell a commercial preparation of phosphorated carbohydrate solution, similar to cola syrup, called Emetrol. Cola drinks allowed to go "flat" have the same antinausea effect. These substances act to soothe the inner lining of the stomach. GINGER also has a calming action on the stomach and can provide relief through drinking flat ginger ale (brands that contain ginger, not just ginger flavoring) or eating small pieces of fresh ginger root.

Treatment for nausea and vomiting also targets any underlying conditions or causative circumstances.

See also ACUPUNCTURE; [MORNING SICKNESS](#); NEUROTRANSMITTER.

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COMMON ANTIEMETIC MEDICATIONS		
Active Ingredient	Representative Products	Availability
bismuth subsalicylate	Pepto-Bismol	over the counter
buclizine	Bucladin-S	requires a doctor's prescription
cyclizine	Marezine	requires a doctor's prescription
dimenhydrinate	Dramamine	over the counter
diphenhydramine	Benadryl	over the counter
dolasetron	Anzemet	requires a doctor's prescription
granisetron	Kytril	requires a doctor's prescription
meclizine	Antivert, Bonine	over the counter (prescription strength also available)
metoclopramide	Reglan	requires a doctor's prescription
ondansetron	Zofran	requires a doctor's prescription
prochlorperazine	Compazine	requires a doctor's prescription
promethazine	Phenergan	requires a doctor's prescription
scopolamine transdermal	Transderm-V	requires a doctor's prescription
trimethobenzamide	Tigan	requires a doctor's prescription

anus The opening through which the body passes solid waste (feces), below the final segment of the COLON and the terminus of the gastrointestinal system. The anal sphincter is a ring of MUSCLE that contracts to contain fecal matter and relaxes to expel it. Learning to control the contraction and relaxation of the anal sphincter begins to take place at age two or three; most children master this control by age four or five. NERVOUS SYSTEM damage, such as with PARKINSON'S DISEASE and sometimes as a consequence of aging, can cause loss of anal sphincter control with resulting FECAL INCONTINENCE.

For further discussion of the anus within the context of gastrointestinal structure and function, please see the overview section "The Gastrointestinal System."

See also [ANAL ATRESIA](#); [ANAL FISSURE](#); [RECTUM](#); [SPINAL CORD INJURY](#); [STROKE](#); [TRAUMATIC BRAIN INJURY \(TBI\)](#).

appendectomy A surgical OPERATION to remove an inflamed or infected APPENDIX. The conventional open procedure involves making an incision two to three inches long in the lower right abdomen. Open appendectomy typically requires two or three days of hospitalization and four to six weeks for full recovery. A laparoscopy appendectomy requires a shorter hospital stay and is a more rapid recovery. For a laparoscopic appendectomy, the surgeon makes four or five small incisions (about ½ inch in length). Through one of the incisions the surgeon inserts the laparoscope, a flexible lighted tube. Through the other incisions the

surgeon inserts special instruments. LAPAROSCOPIC SURGERY often requires only an overnight stay in the hospital, with return to normal activities in three to four weeks. Laparoscopic appendectomy is the operation of choice for most circumstances of simple appendicitis in which INFLAMMATION and INFECTION remain confined to the appendix and the diagnosis is clear-cut. The surgeon may choose to convert a laparoscopic to an open procedure should there be any complicating factors once the surgery begins.

Risks of appendectomy, open or laparoscopic, include leakage of intestinal content into the peritoneal cavity, which can result in PERITONITIS, or postoperative ABSCESS (pocket of infection). To safeguard against these complications, postoperative care includes intravenous ANTIBIOTIC MEDICATIONS during the hospital stay and a course of oral antibiotics following hospital discharge. As with any surgery, reaction to ANESTHESIA and bleeding during or after the operation are also risks. Full recovery after appendectomy for simple appendicitis is the norm, with most people returning to their usual activities within six weeks (up to eight weeks for strenuous physical activity such as competitive sports).

See also [ENDOSCOPY](#).

appendicitis INFLAMMATION of the APPENDIX. Because the appendix is so narrow, inflammation can rapidly cause it to swell closed, trapping BACTERIA-laden intestinal matter. This sets the stage for INFECTION that can spread to involve nearby structures.

Appendicitis is an emergency that requires immediate surgery.

The classic symptoms of appendicitis include

- PAIN in the lower right abdomen
- NAUSEA, VOMITING, and aversion to food
- tendency to lie in somewhat of a fetal position, often on the right side with the knees drawn toward the chest

However, more than a third of people who have appendicitis have atypical symptoms that may include diffuse (generalized) abdominal dis-

comfort, pain referred to the back or shoulder area, or symptoms that mimic other health conditions ranging from DYSPEPSIA (indigestion) to URINARY TRACT INFECTION (UTI). Further, there are no definitive causes of appendicitis, though often the surgeon or pathologist detects particles of food or fecal matter lodged in the appendix. The key risk of appendicitis is that the inflamed appendix may perforate (rupture), spilling intestinal debris and infectious matter into the peritoneal cavity. The resulting widespread contamination evolves quickly to PERITONITIS, a life-threatening infection.

The diagnostic path begins with a physical examination to determine the quality of the pain. Key signs of appendicitis during examination include rebound tenderness (increased pain when the doctor presses slowly downward on the abdomen and then suddenly releases the pressure) and pain (often intense) with pressure applied directly over the location of the appendix. A DIGITAL RECTAL EXAMINATION (DRE) also often elicits a significant pain response. A complete blood count (CBC) may reveal the inflammatory process or an infection.

Surgical removal of an inflamed appendix (APPENDECTOMY) provides the only conclusive diagnosis of appendicitis. ANTIBIOTIC MEDICATIONS generally are not effective in treating appendicitis because the infection is generally well under way by the time of diagnosis and the risk of peritonitis or other complicating factors is very high.

See also [GALLBLADDER DISEASE](#); [PELVIC INFLAMMATORY DISEASE \(PID\)](#).

appendix A small, fingerlike projection, sometimes called the vermiform appendix, extending from the bottom of the CECUM, the first segment of the large intestine (COLON). Historically health professionals have viewed the appendix as a vestigial structure with no functional purpose. However, recent research identifies clusters of GUT-ASSOCIATED LYMPHOID TISSUE (GALT), fragments of lymphoid tissue, within the lining of the appendix. Though researchers do not yet understand the role of GALT, they know it belongs to the IMMUNE SYSTEM and has functions related to the IMMUNE RESPONSE. It appears that the immune functions of the appendix, like those of the THYMUS, are most active early in life. Researchers are studying the relation-

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ship between the appendix and INFLAMMATORY BOWEL DISEASE (IBD) as well as the role of GALT HYPERPLASIA (enlargement of the lymphoid tissue) in APPENDICITIS. Because of its location and narrow structure, the appendix is vulnerable to circumstances that cause it to become inflamed or infected. Appendicitis is the most common health condition involving the appendix.

For further discussion of the appendix within the context of gastrointestinal structure and function, please see the overview section “The Gastrointestinal System.”

See also AGING, EFFECTS ON IMMUNE RESPONSE; [APPENDECTOMY](#); MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT).

ascites The accumulation of fluid within the peritoneal cavity. Ascites is an abnormal condition

that often accompanies chronic LIVER disease such as CIRRHOSIS and LIVER DISEASE OF ALCOHOLISM. Ascites sometimes also develops with HEART FAILURE, END-STAGE RENAL FAILURE (ESRF), OVARIAN CANCER, and metastatic cancer that infiltrates abdominal structures. Ascites typically causes little discomfort. Paracentesis, in which the doctor uses a needle and syringe to withdraw a sample of the fluid, can help to diagnose the cause of the ascites. The doctor also may use paracentesis to withdraw large amounts of fluid to relieve the ascites. Other treatments include a very low sodium diet and diuretic medications to encourage the kidneys to withdraw larger amounts of fluid from the blood. Untreated or persistent ascites invites PERITONITIS, a potentially life-threatening INFECTION.

See also [HEPATITIS](#); [PORTAL HYPERTENSION](#); [STEATO-HEPATITIS](#).

barium enema A diagnostic imaging procedure to examine the structures of the lower gastrointestinal tract including the RECTUM and COLON, sometimes called a lower GI (gastrointestinal) series. The gastroenterologist may request a barium ENEMA to help diagnose intestinal polyps, DIVERTICULAR DISEASE, INFLAMMATORY BOWEL DISEASE (IBS), HIRSCHSPRUNG'S DISEASE, intestinal obstruction, COLORECTAL CANCER, and RECTAL PROLAPSE. Preparation for barium enema typically includes a clear liquid diet for two days before the procedure, a laxative the night before the procedure, and an ENEMA the morning before the procedure to cleanse the colon.

The test consists of a barium mixture administered via enema, followed by a series of X-rays (FLUOROSCOPY). Body position and the heaviness of the barium help the barium mixture to flow upward into the lower gastrointestinal tract. For a single-contrast barium enema, the radiologist takes X-ray images of the barium-filled colon and rectum. For a double-contrast barium enema the person eliminates as much barium as possible after the first series of X-rays, then the radiologist injects a small amount of air into the lower bowel and takes another X-ray series. Double-contrast barium enema provides more detailed visualization. The heaviness and pressure of the barium make the procedure uncomfortable and some people experience cramping. The procedure takes 20 to 45 minutes, with the person placed in different positions to help move the barium through the colon. Light-colored stools are normal for several days after the procedure while the barium clears the body. A rare complication is bowel perforation.

See also BARIUM SWALLOW; COLONOSCOPY; INTES-TINAL POLYP; LAXATIVES.

barium swallow A diagnostic imaging procedure to examine the structures of the upper gastrointestinal tract including the ESOPHAGUS, STOMACH, and DUODENUM (beginning of the SMALL INTESTINE), sometimes called an upper GI (gastrointestinal) series. The gastroenterologist may request a barium swallow to help diagnose HIATAL HERNIA, esophageal obstruction, ESOPHAGEAL SPASM, stomach dysfunction, and PEPTIC ULCER DISEASE. Preparation for barium swallow typically is nothing to eat or drink for 8 to 12 hours, before the procedure.

The test consists of swallowing a preparation of barium, a high-contrast medium, during a series of X-rays (FLUOROSCOPY). The barium lines the structures of the upper gastrointestinal tract, making them visible by X-ray. The barium preparation is about the consistency of a milkshake though chalky in texture. The procedure takes 30 to 60 minutes, with the person placed in different positions to help move the barium through the upper gastrointestinal tract. Some people experience mild CONSTIPATION after the procedure, and it is normal for the stools to be light-colored for several days after the procedure while the barium clears the body.

See also BARIUM ENEMA; ENDOSCOPY.

Barrett's esophagus Changes to the lining of the ESOPHAGUS in which the tissue becomes similar to that of the intestine. The altered tissue is Barrett's esophagus does not itself cause symptoms, though the condition often appears in association with GASTROESOPHAGEAL REFLUX DISORDER (GERD), which does cause symptoms. The key clinical significance of Barrett's esophagus is its association with a rare and deadly form of CANCER, esophageal ADENOCARCINOMA. Though few people who have Barrett's esophagus will develop esophageal adenocarcinoma, nearly everyone who does develop

esophageal adenocarcinoma also has Barrett's esophagus.

Diagnosis of Barrett's esophagus requires endoscopic biopsy of the esophageal lining. Altered tissue often appears reddened in endoscopic visualization, though appearance cannot make the diagnosis as GERD also can cause INFLAMMATION and irritation of the esophageal lining that causes it to appear reddened. A person who has confirmed Barrett's esophagus should undergo periodic endoscopic biopsy as a measure to detect further changes in the tissue (dysplasia) that could indicate a developing cancer. Esophageal adenocarcinoma appears to develop slowly, with a period of years during which the tissue changes are transitional. Dysplasia or cancer requires appropriate treatment, which varies according to individual health circumstances. There are no treatments for Barrett's esophagus or to prevent its conversion to esophageal adenocarcinoma.

See also CANCER RISK FACTORS; [ENDOSCOPY](#); [ESOPHAGEAL CANCER](#); [ESOPHAGITIS](#).

bezoar A hardened mass of indigestible matter that forms in the STOMACH, such as HAIR (trichobezoar), insoluble plant fiber (phytobezoar), or a combination of hair and plant fiber (trichophytobezoar). Bezoars can develop in children who chew their hair or eat substances such as sand or grass and in adults who have slowed gastrointestinal motility, such as might occur with GASTROPARESIS or ACHALASIA. A bezoar can remain undetected in the stomach for months, until it becomes large enough to block the passage of food into the SMALL INTESTINE. Common symptoms include PAIN, NAUSEA, VOMITING, and occasionally a palpable lump. BARIUM SWALLOW or ENDOSCOPY can confirm the diagnosis. Surgery (endoscopic or open) to remove the bezoar is often the only treatment, as by the time a bezoar causes symptoms it is too large to pass through the gastrointestinal tract. Bezoars may recur when the behavior responsible for their development, such as hair chewing, persists.

See also [ILEUS](#).

bile A liquid that the LIVER produces to carry some of its waste products into the digestive tract. Specialized cells called hepatocytes synthesize bile from water, cholesterol, bile acids, bile salts, BILIRUBIN and

other bile pigments, and electrolytes. The hepatocytes break down cholesterol, a fatty acid, into bile acids. Other cells in the liver further convert bile acids into water-soluble forms called bile salts.

The SPLEEN is the body's scavenger and one of its jobs is to remove old erythrocytes (red BLOOD cells) from the blood and break them down. One of the byproducts of this process is heme, the iron compounds. After further metabolism one derivative of heme is bilirubin. Bilirubin is dark yellow and is the primary pigment in bile, giving bile its dominant yellow coloration. Other bile pigments come from substances the liver detoxifies from the blood, adding to the bile's color.

A network of BILE DUCTS collects bile from the liver and carries it to the GALLBLADDER. The walls of the gallbladder absorb about 90 percent of the water the bile contains, producing a greatly concentrated solution that the gallbladder ejects during digestion to aid in digesting fatty foods. Bile that enters the intestinal tract that the body does not need for digestion continues to travel through the intestines, eventually mixing with fecal matter for excretion from the body. The liver secretes about 750 milliliters (roughly a quart) of bile every day.

See also ERYTHROCYTE; CHOLESTEROL BLOOD LEVELS; [GALLBLADDER DISEASE](#); [PANCREATITIS](#).

bile ducts Channels that carry BILE from LIVER to the GALLBLADDER and from the gallbladder to the DUODENUM (first segment of the SMALL INTESTINE). The intrahepatic ducts are within the structure of the liver. They collect bile the liver secretes and transport it from the liver. The extrahepatic ducts are outside the liver and route bile to the gallbladder and duodenum. They are

- the hepatic duct, which carries bile out of the liver to the cystic duct
- the cystic duct, which carries bile from the hepatic duct to the gallbladder and from the gallbladder to the common duct
- the common duct, which carries bile into the duodenum

The health conditions most likely to involve the bile ducts are BILIARY ATRESIA, a CONGENITAL ANOMALY in which the bile ducts form incompletely or not at all, and ductal occlusion resulting from cholelithia-

sis, in which gallstones escape from the gallbladder and lodge in a bile duct, blocking the flow of bile and causing PAIN. CANCER of the bile ducts, called cholangiocarcinoma, occurs though is rare.

For further discussion of the bile ducts within the context of gastrointestinal structure and function, please see the overview section “The Gastrointestinal System.”

See also GALLBLADDER DISEASE; PANCREAS; PRIMARY BILIARY CIRRHOSIS; PRIMARY SCLEROSING CHOLANGITIS.

biliary atresia Absence or malformation of the BILE DUCTS, also called neonatal CHOLESTASIS. Biliary atresia is nearly always congenital (present at birth). In some infants biliary atresia appears to develop as a consequence of an inflammatory process that occurs shortly after birth, destroying the bile ducts. Biliary atresia prevents the flow of BILE from the LIVER, causing toxins to accumulate in the liver. Symptoms depend on the extent of the atresia and may become apparent within days of birth or manifest slowly over the first six months of life. Symptoms include

- JAUNDICE, a yellowish discoloration of the SKIN resulting from the liver’s inability to break down BILIRUBIN into components the body can excrete as waste
- stools that are pale in color, the consistency of clay, and unusually foul smelling
- dark URINE
- failure to grow or gain weight
- ABDOMINAL DISTENTION resulting from enlarged SPLEEN
- fussiness and irritability

NEONATAL JAUNDICE

NEONATAL JAUNDICE is fairly common, affecting about 50 percent of full-term and 80 percent of preterm (premature) newborns. It points to biliary atresia or other LIVER conditions only when it is apparent within the first 24 hours after birth or persists despite treatment.

The diagnostic path includes blood tests to measure the amounts of bilirubin in the blood and PERCUTANEOUS LIVER BIOPSY to determine whether the hepatocytes, the cells that process bilirubin, are nor-

mal. Normal hepatocytes strongly suggest biliary atresia. Other diagnostic procedures may include ULTRASOUND and intraoperative cholangiography (injecting dye into the bile ducts to visualize them using FLUOROSCOPY or other imaging technologies).

The only treatments for biliary atresia are surgical procedures to help restore the flow of bile. The first of these procedures is hepatic portoenterostomy, in which the surgeon creates an opening between the JEJUNUM (middle segment of the SMALL INTESTINE) and the bile duct structures that exist outside the liver. This procedure allows bile to drain directly from the liver into the small intestine and can achieve adequate liver function for up to several years. However, it does not correct the structural defects of the bile transport network within the liver, and damage to the liver (fibrosis and CIRRHOSIS) continues. Nearly all infants who have biliary atresia require LIVER TRANSPLANTATION, the second surgical procedure to treat the condition, before they are three years old. Long-term success of liver transplantation depends on numerous variables.

See also CONGENITAL ANOMALY; LIVER FAILURE.

bilirubin A metabolic product of ERYTHROCYTE (red BLOOD cell) heme that is a key component of HEMOGLOBIN. Bilirubin exists in two forms, conjugated (also called direct), which is water soluble, and unconjugated (also called indirect or free), which is fat soluble. The amounts and ratios of bilirubin present in the BLOOD help doctors assess LIVER and GALLBLADDER functions.

NORMAL BLOOD BILIRUBIN VALUES

unconjugated (indirect) bilirubin	0.1 to 1.0 milligrams per deciliter (mg/dL)
conjugated (direct) bilirubin	0.0 to 0.4 mg/dL
total bilirubin	0.3 to 1.9 mg/dL

The SPLEEN removes old erythrocytes (red blood cells), which contain high concentrations of hemoglobin, from the circulation and begins to break them down into their components. The bilirubin that results from this process is unconjugated, a form the body cannot eliminate. ALBUMIN, a protein in the blood, transports this unconjugated bilirubin to the liver. There, actions of an enzyme—glucuronyl transferase—help a chemical

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reaction that converts the unconjugated bilirubin to conjugated bilirubin, which then becomes an ingredient of BILE.

Bilirubin is yellow and in turn colors the bile yellow; hence its designation as a bile pigment. Intestinal BACTERIA further metabolize bilirubin, the major component of which is urobilinogen. Urobilinogen gives the feces their characteristic dark color. Pale feces are a hallmark of disturbances of bilirubin METABOLISM. Increased bilirubin levels in the blood result in JAUNDICE, a yellowish discoloration of the SKIN most visible in the SCLERA (“white” of the EYE). Certain wavelengths of light on the skin help the body complete bilirubin metabolism.

See also CIRRHOSIS; HEPATITIS; PHOTOTHERAPY.

biliary dysfunction See GALLBLADDER DISEASE.

borborygmus The growling and rumbling sound of gas moving through the gastrointestinal tract during digestion. Borborygmus, sometimes referred to in the plural, *borborygmi*, indicates normal function of the gastrointestinal system. The sounds originate with the STOMACH and continue through the SMALL INTESTINE and large intestine. Excessive rumblings may indicate incomplete digestion such as may result from eating too rapidly or eating too much at one time. Some people experience an increase in borborygmus when they are hungry.

See also BOWEL SOUNDS; FLATULENCE.

bowel atresia A CONGENITAL ANOMALY in which there is incomplete development of the intestinal tract, typically with closures and “dead ends” that block flow through the intestines. The intestines may be entangled or intussuscepted (one segment of bowel telescopes into another), presenting grave risk for tissue death (necrosis). Nearly always the diagnosis is apparent within hours of birth because the infant is unable to eat and the abdomen quickly becomes distended. VOMITING BILE is a key indicator of intestinal obstruction of some sort. Bowel atresia is more common in premature infants. The most common locations for bowel atresia are the DUODENUM (duodenal atresia) and the JEJUNUM and ILEUM (jejunoileal atresia). Bowel atresia is life-threatening and requires emergency surgery to correct the defects.

See also ANAL ATRESIA; CONGENITAL HEART DISEASE; ESOPHAGEAL ATRESIA; INTUSSUSCEPTION.

bowel movement The passage of solid digestive waste (called feces or stool) from the body through the ANUS. The frequency, appearance, and nature of bowel movements are highly variable. Food typically travels through the gastrointestinal system in 18 to 36 hours, so most people have bowel movements daily or every other day. However, “normal” is an individual pattern that correlates to dietary habits, physical activity level, and lifestyle and can range from three bowel movements a day to one bowel movement every three days. What can become significant from a health standpoint are deviations from an individual’s pattern of bowel movements. Short-term changes in bowel patterns may result from eating different foods, viral INFECTION (GASTROENTERITIS OR ENTERITIS), inadequate fluid consumption, and medications. A shift in bowel patterns not due to intentional actions such as dietary or exercise change may indicate health conditions that require medical evaluation.

See also BOWEL SOUNDS; CONSTIPATION; DIARRHEA.

bowel sounds The noises of the gastrointestinal tract. Listening to bowel sounds through a stethoscope (AUSCULTATION) provides important clues about the function of the gastrointestinal tract. Normal bowel sounds vary in tone and loudness according to the activity of the bowel though follow characteristic patterns the doctor can identify. Excessive bowel sounds often accompany excessive bowel activity such as DIARRHEA, GASTROENTERITIS, and flare-ups of INFLAMMATORY BOWEL DISEASE (IBD). Reduced bowel sounds occur when bowel activity slows, such as between meals or when there is an intestinal obstruction. Narcotic medications and anesthetic agents also slow bowel function, and reduced bowel sounds may persist for several days after surgery. The absence of bowel sounds signals a nonfunctioning bowel, which can be due to intestinal obstruction or, in an infant, a gastrointestinal atresia. The absence of bowel sounds may be a sign of a medical emergency that requires surgical intervention.

See also BORBORYGMUS; BOWEL ATRESIA; ESOPHAGEAL ATRESIA.



cecum The first segment of the COLON (large intestine) into which the ILEUM, the final segment of the SMALL INTESTINE, empties digestive matter. The cecum is a pouchlike structure located in the lower right abdomen that absorbs water from the waste, returning fluid to the body and consolidating the waste for its journey through the end stage of digestion. The rhythmic contractions of PERISTALSIS move the remaining solid waste into the remainder of the colon. The APPENDIX extends from the bottom of the cecum.

For further discussion of the cecum and the colon within the context of gastrointestinal structure and function, please see the overview section “The Gastrointestinal System.”

See also [ANUS](#); [RECTUM](#).

celiac disease A condition affecting the SMALL INTESTINE in which consuming foods that contain gluten, a plant protein prominent in wheat, triggers an inflammatory response that prevents the intestinal mucosa (lining) from absorbing NUTRIENTS. Gluten, and more specifically proteins it contains called gliadins, acts as an ANTIGEN to initiate a localized IMMUNE RESPONSE. Researchers believe celiac disease has a genetic foundation, though the specific GENE or genes responsible remain undetermined. Though severe celiac disease can cause significant NUTRITIONAL DEFICIENCIES that affect growth, FERTILITY, and overall health, most people who adopt a gluten-free diet are able to avert the inflammatory episodes and minimize damage to the intestinal mucosa. About 1 in 5,000 Americans has celiac disease.

Symptoms and Diagnostic Path

Symptoms appear in celiac disease with exposure to gluten, so usually do not become apparent until

after the age of two years when children begin eating solid foods. People who have celiac disease experience a broad range of symptoms, with some people having virtually no indications they have celiac disease until nutritional deficiencies become problematic and other people suffering chronic DIARRHEA, cramping, ABDOMINAL DISTENTION, and other gastrointestinal disruptions. Some people have outbreaks of DERMATITIS herpetiformis, an itchy SKIN RASH. An early indication of celiac disease, especially in children, is the passing of large, loose, light-colored, foul-smelling stools, which suggests high fat excretion (STEATORRHEA) characteristic of MALABSORPTION.

Celiac disease may affect any or all of the segments of the small intestine, and the degree to which it affects them determines the symptoms. Many of the symptoms and signs of celiac disease arise from health problems due to nutritional deficiencies that correlate to the segment of small intestine affected, manifesting in conditions such as ANEMIA (deficiency of iron, suggesting involvement of the DUODENUM and upper JEJUNUM) and frequent nosebleeds (deficiency of VITAMIN K, suggesting involvement of the lower jejunum and the ILEUM). Children who have celiac disease may also appear malnourished, showing spindly limbs and protruding bellies, despite adequate food consumption.

Biopsy of the intestinal mucosa in people who have celiac disease tends to show marked structural differences from normal intestinal mucosa. Most significant is flattening of the mucosal tissue from its normal “pleated” appearance, which reduces the surface area available for nutrient absorption. Lymphocytes and leukocytes are also present within the mucosal tissue, evidence of the inflammatory process. However, there are no definitive tests to diagnose celiac disease. BLOOD

tests to measure ANTIBODY levels and biopsy of the intestinal mucosa provide strong, though not conclusive, evidence of celiac disease. Antibody levels become elevated only during active episodes of the disease, and biopsy samples may not represent the overall status of the small intestine.

The gastroenterologist considers these results in conjunction with the pattern of symptoms, FAMILY MEDICAL PEDIGREE, and response to a gluten-free diet. Symptoms that disappear with a gluten-free diet provide fairly conclusive diagnosis, though this marker is useful only in people who have obvious gastrointestinal or dermatologic symptoms.

Treatment Options and Outlook

The primary treatment for celiac disease is a gluten-free diet. This means eliminating all wheat and wheat products, as well as numerous processed foods that contain gluten as filler. Many foods that restaurants serve also contain gluten, requiring great diligence to determine food ingredients. Wheat-free products may still contain gluten. Some people also need to eliminate oats, barley, and rye and products made from them, as these grains contain small amounts of gluten. People who have severe celiac disease may require NUTRITIONAL SUPPLEMENTS or nutritional-replacement therapies. Most people who follow a gluten-free diet experience improvement within two weeks and an end to their symptoms within a few months. The longer there are no symptoms, the more the intestinal mucosa restores itself and often returns to normal in people who remain symptom-free for several years.

Risk Factors and Preventive Measures

Celiac disease appears to be genetic, and as yet researchers do not know what, if any, risk factors exist. Many people are able to control their symptoms and prevent disease flareups by avoiding foods that trigger them. The doctor also may recommend nutritional supplements to minimize or prevent nutritional deficiencies.

See also HUMAN LEUKOCYTE ANTIGENS (HLAS); INFLAMMATORY BOWEL DISEASE (IBD); IRRITABLE BOWEL SYNDROME (IBS); LEUKOCYTE; LYMPHOCYTE; MAJOR HISTOCOMPATIBILITY COMPLEX (MHC); MALNUTRITION; MINERALS AND HEALTH; NUTRITIONAL NEEDS; VITAMINS AND HEALTH.

cholecystectomy A surgical OPERATION to remove the GALLBLADDER. Cholecystectomy is the most common treatment in the United States for GALLBLADDER DISEASE including gallstones (cholelithiasis), cholecystitis (INFLAMMATION OR INFECTION of the gallbladder), and biliary dyskinesia (diminished ability of the gallbladder to eject BILE). About 500,000 Americans undergo cholecystectomy each year.

Surgical Procedure

There are two methods for performing cholecystectomy, laparoscopic and open. About 95 percent of cholecystectomies surgeons perform in the United States are laparoscopic. Surgeons perform open cholecystectomy, once the standard, only when there are contraindications for laparoscopic cholecystectomy (such as extreme OBESITY) or laparoscopic cholecystectomy cannot successfully remove the gallbladder (such as when there are many stones or there is extensive scarring from long-standing gallbladder disease or repeated infections). Both operations require general ANESTHESIA and an overnight stay in the hospital.

Laparoscopic cholecystectomy In laparoscopic cholecystectomy the surgeon makes four or five small incisions and inserts a laparoscope and tiny instruments through them. The surgeon operates by visualizing the gallbladder via closed-circuit television display. The operation takes 45 to 60 minutes. Most people then stay several hours in the recovery room and overnight in the hospital. After surgery, many people returning to regular daily activities (except strenuous physical exercise) within three weeks, though full recovery takes six to eight weeks.

Open cholecystectomy This procedure is major surgery. The surgeon makes an incision 5 to 8 inches long through the abdominal muscles to expose the LIVER and the gallbladder beneath it. The operation takes about two hours. Most people then stay five to seven days in the hospital. Many people can return to light activity in about four weeks. Full recovery after open cholecystectomy takes about 12 weeks.

Risks and Complications

The primary risks of either operation are bleeding, anesthesia reaction, damage to the bile ducts and other adjacent organs and structures, and postop-

erative infection. The surgeon often administers preoperative and postoperative doses of ANTIBIOTIC MEDICATIONS as a prophylactic measure for infection. Factors that can complicate or slow recovery include DIABETES, OBESITY, and bleeding or clotting disorders. For reasons doctors do not fully understand, 15 to 20 percent of people who undergo cholecystectomy (either laparoscopic or open) continue to experience symptoms similar to those of gallbladder disease even after surgery, called postcholecystectomy syndrome. Occasionally gallstones can escape from the gallbladder during surgery and become trapped in the common bile duct or cystic bile duct, requiring a follow-up procedure, typically ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP), to remove them. Rarely, gallstones can form in the bile ducts months to years after cholecystectomy.

Postoperative infection is a significant risk with open cholecystectomy and in people who have diabetes or obesity, as these conditions can impair HEALING. Warning signs of infection include

- increased PAIN at the incision site
- pain elsewhere in the abdomen
- drainage from the incision site
- FEVER (temperature above 101°F)
- NAUSEA and VOMITING

Prompt antibiotic therapy successfully treats most postoperative infections. Persistent infection or delayed treatment may result in an ABSCESS that requires additional surgery to open and drain the infection.

BENEFITS AND RISKS OF CHOLECYSTECTOMY

Benefits	Risks
ends symptoms	intraoperative or
restores normal digestion	postoperative bleeding
averts symptom-related complications	ANESTHESIA reaction
	postoperative PAIN
	postoperative INFECTION
	inadvertent damage to LIVER and other structures
	scarring and adhesions
	postcholecystectomy syndrome

Outlook and Lifestyle Modifications

Cholecystectomy eliminates symptoms in about 80 percent of people who have gallbladder disease. Most people return to the same lifestyle habits as before surgery, including eating. The liver continues to manufacture bile, which flows directly into the small intestine. The body adapts to the weaker concentration of this bile within a few weeks of the cholecystectomy, and digestion returns to normal. Some people find that high-fat meals generate mild to moderate gastrointestinal distress or mimic gallbladder disease symptoms for several months after surgery. People who undergo open cholecystectomy may be unable to participate in strenuous physical activities for up to six months while the abdominal muscles regain STRENGTH.

See also [HEPATIC ABSCESS](#); [JAUNDICE](#); SURGERY BENEFIT AND RISK ASSESSMENT.

cholecystitis See [GALLBLADDER DISEASE](#).

cholelithiasis See [GALLBLADDER DISEASE](#).

cholestasis Inadequate or lack of BILE flow resulting from either obstruction of the BILE DUCTS or dysfunctions of the LIVER. Common symptoms of cholestasis include

- JAUNDICE (yellow discoloration of the SKIN)
- PRURITUS (generalized itching)
- easy bruising
- pale stools and dark URINE
- xanthomas (fatty deposits in the dermis layer of the skin)

CONDITIONS THAT CAN CAUSE CHOLESTASIS

BILIARY ATRESIA	gallstones
HEPATITIS	HEPATOTOXINS
LIVER DISEASE OF ALCOHOLISM	medication SIDE EFFECTS
obstructed BILE DUCTS	PANCREATIC CANCER
PANCREATITIS	PRIMARY BILIARY CIRRHOSIS

The diagnostic path includes blood tests to confirm the cholestasis, typically the levels of BILIRUBIN and the enzyme alkaline phosphatase, both of which become elevated with cholestasis. Other diagnostic procedures may include ULTRASOUND,

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COMPUTED TOMOGRAPHY (CT) SCAN, and PERCUTANEOUS LIVER BIOPSY. Treatment targets the underlying cause or condition.

Longstanding cholestasis can result in deficiencies of fat-soluble vitamins, notably vitamin D and VITAMIN K, as the SMALL INTESTINE needs bile to digest fats.

See also ALCOHOLISM; LIVER FAILURE; XANTHOMA.

cholesterol, endogenous A sterol ALCOHOL molecule essential for many functions of cellular METABOLISM and the synthesis (production) of numerous hormones. The LIVER synthesizes the cholesterol that circulates within the body (endogenous) from dietary fats, particularly saturated fats, and the components of dietary cholesterol that enter the bloodstream from the gastrointestinal tract. The liver can continue to synthesize cholesterol as long as it receives the ingredients to do so, under genetically mediated regulation.

Because cholesterol is fat soluble it does not dissolve in the blood, so lipoproteins bind with cholesterol to transport it through the bloodstream. Excessive amounts of cholesterol in the bloodstream contribute to cardiovascular conditions such as ATHEROSCLEROSIS and CORONARY ARTERY DISEASE (CAD). Inadequate amounts of cholesterol in the body are uncommon though occur with conditions such as myelogenous LEUKEMIA and AIDS. Low cholesterol prevents cells from repairing themselves and also the body unable to produce “stress” hormones, such as CORTISOL that are essential for IMMUNE RESPONSE. The liver also uses cholesterol to synthesize BILE, which carries cholesterol into the gastrointestinal tract for reabsorption and recycling or elimination. Various endocrine glands use cholesterol to synthesize STEROID hormones, such as the ADRENAL GLANDS, which produce cortisol, and the gonads (sex glands), which produce TESTOSTERONE and ESTROGENS. Cells throughout the body use cholesterol for cell membrane repair.

See also CHOLESTEROL BLOOD LEVELS; CHOLESTEROL, DIETARY; HIV/AIDS; HYPERLIPIDEMIA; LIFESTYLE AND HEALTH; STRESS RESPONSE HORMONAL CASCADE.

cirrhosis A progressive condition in which fibrous tissue replaces damaged LIVER tissue, usu-

ally over an extended time and as a result of continued injury to the liver. The scarring is permanent and interferes with the liver’s ability to function, eventually resulting in LIVER FAILURE. Numerous circumstances and health conditions can result in cirrhosis. The most common causes of cirrhosis are HEPATITIS, LIVER DISEASE OF ALCOHOLISM, chronic dysfunction of the BILE system, STEATOHEPATITIS, and HEPATOTOXINS. Cirrhosis is the leading reason for LIVER TRANSPLANTATION, the only treatment for end-stage cirrhosis and resulting liver failure.

Symptoms and Diagnostic Path

In its mild to moderate stages, cirrhosis often does not show symptoms or generates vague symptoms that suggest a variety of causes. Until cirrhosis becomes fairly advanced, even BLOOD tests that measure liver enzymes (a hallmark of liver function) and diagnostic imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN often show normal findings. When symptoms become apparent, the cirrhosis has significantly compromised liver function, and numerous changes occur throughout the body. Indications of these changes often include

- edema (swelling of the limbs) and ASCITES (fluid accumulation in the abdominal cavity) resulting from PORTAL HYPERTENSION (increased resistance to blood flow through the liver) and RENAL FAILURE (kidney dysfunction)
- JAUNDICE (yellow discoloration of the SKIN) and PRURITIS (extreme itching of the skin) resulting from the liver’s inability to metabolize HEMOGLOBIN and synthesize bile, which allows BILIRUBIN concentrations in the blood to rise
- easy bruising and prolonged bleeding due to the liver’s inability to synthesize CLOTTING FACTORS and produce enough bile to metabolize the dietary fats necessary for absorbing VITAMIN K
- lack of APPETITE, resulting from diminished bile production, and corresponding unintended weight loss
- INSULIN RESISTANCE or type 2 DIABETES resulting from the liver’s inability to properly metabolize cholesterol and manage GLUCOSE (sugar) storage and retrieval

- **GYNECOMASTIA** (enlarged breasts) in men and **AMENORRHEA** (absence of menstrual periods) in women due to the diminished ability of the liver to metabolize **ESTROGENS**

The liver may feel enlarged or irregular when the gastroenterologist palpates the abdomen. By this stage, numerous blood chemistry tests show abnormal results. **PERCUTANEOUS LIVER BIOPSY** confirms the presence of fibrous tissue and the diagnosis of cirrhosis.

Treatment Options and Outlook

Treatment attempts to manage symptoms, address consequential health problems, and slow the progression of any underlying health conditions. Eliminating **ALCOHOL** consumption, medications, and environmental exposures that damage liver cells are among the measures essential to preserve remaining liver function. Numerous clinical studies show the ability of the herbal product **MILK THISTLE** or silymarin, its active ingredient, to help protect the liver from further damage. When cirrhosis progresses despite these interventions, liver transplantation becomes the treatment of final resort. Without liver transplantation, progressive cirrhosis is fatal. Liver transplantation permanently resolves cirrhosis, though at present there are far fewer donor livers available than people who need them. Live donor liver segment donation, in which a living person donates a portion of his or her healthy liver, is an option to full liver transplantation when a donor is available.

Risk Factors and Preventive Measures

Cirrhosis results from chronic, long-term damage to the liver. People who are at risk for developing cirrhosis have longstanding liver disease, such as chronic hepatitis, hepatitis of **ALCOHOLISM**, **HEMOCHROMATOSIS**, **PRIMARY BILIARY CIRRHOSIS**, **PRIMARY SCLEROSING CHOLANGITIS**, and **WILSON'S DISEASE**. Preventive measures include vaccination against hepatitis infection (hepatitis A and hepatitis B) and minimizing behaviors that allow exposure to hepatitis. Consistent **PERSONAL HYGIENE** practices, such as **HAND WASHING** before handling food and after going to the bathroom, help control the spread of the hepatitis virus.

See also **HEPATITIS PREVENTION; LIFESTYLE AND HEALTH; ORGAN TRANSPLANTATION**.

colitis **INFLAMMATION** of the **COLON**. Colitis can be acute (sudden) or chronic (long-term). Various circumstances can cause acute colitis. Among them are **INFECTION**, radiation, and ischemia. Chronic colitis is usually a form of **INFLAMMATORY BOWEL DISEASE (IBD)**, an autoimmune disorder. The symptoms of colitis are abdominal discomfort, cramping, and **DIARRHEA**. The doctor makes the diagnosis primarily on the basis of symptoms; **BLOOD** tests often can confirm the presence of pathogens. Treatment may include medications that target the underlying cause of the inflammation or infection as well as antidiarrheal medications.

Infectious Colitis

Bacterial and protozoan infections of the colon are common. People who are already debilitated—such as the very old, the very young, and those with compromised immune function—face increased risk for complications, such as **DEHYDRATION**, that can be fatal. Fecal cultures can identify the causative agent, which then determines the appropriate treatment.

Bacterial colitis Numerous **BACTERIA** cause bacterial infections of the colon, which often are **FOOD-BORNE ILLNESSES**. Those most frequently detected include *Salmonella*, *Shigella*, *Campylobacter jejuni*, and *Listeria monocytogenes*. Treatment for bacterial colitis is the appropriate antibiotic medication, which helps contain symptoms within 48 to 72 hours and eliminate the infection in about 10 to 14 days. Bacterial infections, notably **LISTERIOSIS**, can be especially dangerous for pregnant women.

Parasites Parasitic infections can occur from drinking contaminated water, eating contaminated foods, and through contact with someone who has such an infection. It is possible to have a protozoan or parasitic infection and show no symptoms. The most common infective protozoan is *Entamoeba histolytica*, which causes **AMEBIASIS** (also called amoebic dysentery). Treatment is a course of antiparasitic medication such as metronidazole. Recovery is usually complete with appropriate treatment. Other protozoan infections include **GIARDIASIS**, **CYCLOSPORIASIS**, and **CRYPTOSPORIDIASIS**.

Radiation Colitis

RADIATION THERAPY to treat cancers, such as **PROSTATE CANCER**, in the lower abdominal region

(pelvic area) can damage the colon, causing symptoms such as diarrhea and cramping. Symptoms typically resolve as the damaged tissue regenerates. Treatment targets symptom relief. Radiation colitis typically resolves when radiation therapy ends.

Ischemic Colitis

Impaired blood flow to the intestinal tract, such as might occur with serious ATHEROSCLEROSIS, can impede intestinal function. Ischemic colitis is most common in people age 70 and older. Treatment focuses on restoring adequate circulation and minimizing symptoms, such as diarrhea, that can result in nutritional deficits and dehydration.

Inflammatory Bowel Disease (IBD)

Chronic inflammation of the colon takes the form of ulcerative colitis or Crohn’s disease, collectively called IBD. Crohn’s disease can affect the entire gastrointestinal tract but most commonly involves the terminal ileum and the ascending colon. Ulcerative colitis can affect the whole colon but usually starts in the rectum and left colon. IBD is an autoimmune disorder in which the IMMUNE SYSTEM attacks sections of the intestinal tract and destroys the mucus lining. This creates ulcerations that cause PAIN, diarrhea, and MALABSORPTION. Treatment for inflammatory colitis typically includes CORTICOSTEROID MEDICATIONS and sometimes immunosuppressive agents such as methotrexate or cyclosporine to suppress the IMMUNE RESPONSE. IBD is a serious and lifelong disorder that requires continuous management through medications and diet.

See also ANTIBIOTIC MEDICATIONS; AUTOIMMUNE DISORDERS; ENTERITIS; FOOD SAFETY; GASTRITIS; GASTROENTERITIS; INCUBATION PERIOD; IRRITABLE BOWEL SYNDROME (IBS); NUTRITIONAL NEEDS; NUTRITIONAL SUPPLEMENTS; PATHOGEN; PERSONAL HYGIENE; PROCTITIS; VIRUS; WATER SAFETY.

colon The large intestine, which extracts water from and consolidates the waste byproducts of digestion. The colon extends from the ILEUM, the final segment of the SMALL INTESTINE, to the ANUS, the exit from the body for solid digestive waste (feces or stool). The colon goes up the left side of the abdomen (the ascending colon), across the

abdomen at the lower ribs (the transverse colon), and down the right side of the abdomen to about the level of the hip JOINT (the descending colon). The final segments of the colon are the sigmoid colon and the RECTUM. The colon is about five feet long in the average adult.

COMMON CONDITIONS AFFECTING THE COLON

COLITIS	COLORECTAL CANCER
CONSTIPATION	Crohn’s disease
DIARRHEA	DIVERTICULAR DISEASE
FECAL IMPACTION	FECAL INCONTINENCE
HIRSCHSPRUNG’S DISEASE	ILEUS
INFLAMMATORY BOWEL DISEASE (IBD)	INTESTINAL POLYP
IRRITABLE BOWEL SYNDROME (IBS)	PROCTITIS
RECTAL FISTULA	RECTAL PROLAPSE
TOXIC MEGACOLON	ulcerative colitis

For further discussion of the colon within the context of gastrointestinal structure and function, please see the overview section “The Gastrointestinal System.”

See also ANAL ATRESIA; ANAL FISSURE; BORBORYG-MUS; BOWEL ATRESIA; BOWEL SOUNDS; COLONOSCOPY; STOMACH.

colonoscopy An examination of the COLON (also called bowel or large intestine) to detect and remove INTESTINAL POLYPS, fleshy growths that may become cancerous, and to biopsy or remove small adenocarcinomas (cancerous polyps). Conventional colonoscopy is an endoscopic procedure in which the gastroenterologist inserts a flexible, lighted tube (endoscope or colonoscope) through the ANUS and into the large intestine.

Reasons for Doing This Test

Colonoscopy is a diagnostic procedure to detect intestinal polyps, COLORECTAL CANCER, and other conditions affecting the colon. Cancer experts believe screening colonoscopy, performed at age 50 (or earlier, when there is family history of colorectal cancer) and every 5 to 10 years thereafter, can prevent 80 to 90 percent of colorectal cancers.

Preparation, Procedure, and Recovery

The gastroenterologist performs conventional colonoscopy in an ENDOSCOPY center or hospital unit, with intravenous general sedation to mini-

mize discomfort and anxiety. The procedure takes 30 to 45 minutes, with another one to two hours to recover from the sedation.

Preparation Most people find the preparation for colonoscopy, which consists of cleansing the gastrointestinal tract, the most unpleasant aspect of the procedure. The preparation for virtual colonoscopy requires the same bowel-cleansing procedure as does conventional colonoscopy. Completing the preparation for colonoscopy is essential for optimal results, however. It typically includes

- no aspirin or aspirin products (to reduce the risk for bleeding) and no iron supplements or products (iron darkens tissue) for five days before the colonoscopy
- no nuts, seeds, grapes, peas, beans, or tomatoes for three days before the colonoscopy (particles from these foods lodge in the folds of the intestinal mucosa)
- NO NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) for five to seven days before the colonoscopy (to reduce the risk for bleeding)
- only clear liquids for 24 hours before the colonoscopy
- at midday the day before the colonoscopy, the bowel-cleansing process begins with the drinking of a laxative solution consumed at the rate of eight ounces every 10 minutes for a total consumption of one gallon of the solution

The laxative prep results in bowel movements that start about an hour after beginning to drink the solution and continue for about eight hours. Drinking the solution often causes NAUSEA. Keeping the solution as cold as possible (even surrounding it with ice in the refrigerator) and chewing gum or sucking on hard candy between glasses can help. It is necessary to drink the entire gallon of the solution to completely clear the gastrointestinal tract. Fecal remnants in the colon can obscure the wall of the bowel, limiting the ability of the gastroenterologist to visualize the entire colon. Most gastroenterologists will not proceed with the colonoscopy if the preparation is incomplete.

Procedure The person lies on his or her left side on a narrow bed, with the knees flexed. After

initiating intravenous sedation, the gastroenterologist gently inserts the lubricated colonoscope into the anus. A small pump injects air ahead of the scope, opening the colon so the gastroenterologist can advance it into the colon. The examination of the colon takes about 20 minutes, longer when there are polyps for the gastroenterologist to remove or biopsy. Some people feel pressure with the injection of air or when the scope rounds the corners of the colon. However, most people feel little discomfort and cannot recall the procedure when it is over.

Recovery Following conventional colonoscopy, the person rests in a recovery area until the sedative wears off, usually within an hour or two, and then may go home. Doctors recommend resting quietly for the remainder of the day, which is what most people feel like doing. There is usually no discomfort after the procedure, aside from an accumulation of intestinal gas until regular eating returns the gastrointestinal tract to normal function. The gastroenterologist receives the pathologist's analysis of any tissues removed within about a week. Following virtual colonoscopy, the person may go home immediately after the procedure.

Risks and Complications

Complications related to conventional colonoscopy are very rare but may include perforated bowel (which requires emergency surgery to repair), INFECTION, and bleeding from removed or biopsied polyps.

Virtual Colonoscopy

Virtual colonoscopy, a procedure that allows non-invasive visualization of the gastrointestinal tract, became available in the late 1990s. Virtual colonoscopy, correctly called computed tomography colonography or CT colonography, uses COMPUTED TOMOGRAPHY (CT) SCAN to examine the colon with nearly the same accuracy as conventional colonoscopy but without the need for sedation or to enter the body.

The significant drawback to CT colonography is that it allows only viewing of the colon, not biopsy or polypectomy. The gastroenterologist must still use conventional colonoscopy to remove detected intestinal polyps or to biopsy suspicious growths. The preparation for virtual colonoscopy

requires the same bowel cleansing procedure as does conventional colonoscopy.

Virtual colonoscopy does not require sedation. For the procedure, the radiologist inserts a small tube into the rectum for the injection of air to open the colon for improved visualization, which may cause discomfort that feels like intestinal gas. Over a period of 10 to 20 minutes the CT scanner takes sequential X-rays while the person lies on his or her back and then STOMACH. A computer compiles the X-rays to create three-dimensional images of the colon.

See also [BARIUM ENEMA](#); [CANCER PREVENTION](#); [INTESTINAL POLYP](#).

colorectal cancer Malignant growths in the COLON, most commonly in the sigmoid colon and the RECTUM. Colorectal cancer is the second-leading cause of death due to CANCER in the United States. However, colorectal cancer is also one of the most preventable and, with early detection, among the most treatable kinds of cancer. More than 95 percent of primary colorectal cancer is ADENOCARCINOMA, a form of cancer in which abnormal but otherwise benign growths (adenomas) become cancerous. Intestinal polyps are adenomas that develop in the colon, growing from the mucous membrane that lines the colon. Intestinal polyps become more common with increasing age, and by age 50, about half of American adults are likely to have them.

TYPES OF POLYPS

There are two common types of colon polyps: adenomas, which are neoplastic (abnormal growths that have no useful function within the body) and have malignant potential, and hyperplastic, which are not neoplastic and have no malignant potential.

A polyp takes 5 to 10 years to grow from microscopic to detectable, and up to several decades to become cancerous, if that is its course. People who have no exceptional risk factors for colorectal cancer typically have a window of 5 to 10 years during which the polyp's cell structure is transitional. Doctors consider such a polyp precancerous. Though only a small percentage of intestinal polyps will become cancerous, there is no way to distin-

guish those that will from those that will remain benign. As a precaution doctors recommend removing all intestinal polyps, which eliminates any concerns about their potential malignancy.

Symptoms and Diagnostic Path

Early colorectal cancer has few, if any, symptoms, further emphasizing the importance of regular screening. When present, symptoms often indicate a cancer that is moderately to significantly advanced and include

- a change in bowel habits or the nature of bowel movements
- unexplained NAUSEA, VOMITING, DIARRHEA, or CONSTIPATION
- rectal bleeding (may be patches of dark discoloration or bright bleeding)
- sensations of abdominal fullness or bloating
- tiredness and fatigue
- unintended weight loss
- ABDOMINAL DISTENTION and pain

The most effective way to detect and diagnose colorectal cancer is through regular screening procedures, which may include

- DIGITAL RECTAL EXAMINATION (DRE), in which the doctor inserts a gloved, lubricated finger into the rectum via the ANUS to feel for abnormalities
- FECAL OCCULT BLOOD TEST (FOBT), in which a laboratory tests a stool sample for microscopic blood (home-testing kits are also available)
- double-contrast BARIUM ENEMA, in which the radiologist instills barium into the lower colon via an ENEMA, then takes X-rays as the barium fills the rectum and sigmoid colon
- sigmoidoscopy, in which the doctor inserts a lighted viewing tube (rigid or flexible) through the anus into the rectum and sigmoid colon, the two segments of the colon nearest the end of the intestinal tract and the sites where more than half of colorectal cancers originate
- COLONOSCOPY, in which the doctor inserts a lighted, flexible viewing tube through the anus and into the entire colon (done under sedation)
- virtual colonoscopy (CT colonography)

Sigmoidoscopy (for the lower colon) and colonoscopy (for the full length of the colon) allow the gastroenterologist to detect and remove intestinal polyps and to biopsy suspicious growths. The gastroenterologist may use colonoscopy to explore suspicious findings from other screening procedures. Further diagnostic procedures may include transrectal or abdominal ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, and MAGNETIC RESONANCE IMAGING (MRI).

Pathology examination of the suspect tissue confirms the diagnosis and establishes the extent of the cancer, a clinical classification process called STAGING OF CANCER. Staging identifies how far the cancer has spread, determines treatment recommendations and protocols, and establishes expectations about how the cancer will respond to treatment (prognosis). The higher the stage number, the more advanced the cancer.

Treatment Options and Outlook

Surgery is the first course of treatment for nearly all colorectal cancers. In cancers detected early, surgery often cures the cancer. Depending on the location and extent of the cancer, the surgeon can

usually remove the cancerous tissue (called a bowel resection) and reconnect the healthy ends of the colon so the colon continues to function normally. Sometimes the colon needs first to heal from the resection, in which case the surgeon performs a temporary COLOSTOMY that allows the colon to pass fecal matter through an opening created in the abdomen. When the colon heals, the surgeon reconnects the ends and closes the colostomy. Extensive cancer may make necessary a permanent colostomy.

The oncologist may recommend RADIATION THERAPY to shrink large tumors before surgery or to kill any cancerous cells remaining after surgery, primarily for cancer located in the rectum. CHEMOTHERAPY kills cancer cells that may have spread beyond the local tumor, and is the follow-up treatment of choice for cancers that involve LYMPH NODES. Often the oncologist will recommend a combination of therapies. Oncologists also typically offer people who have stage 2 through stage 4 colorectal cancer the opportunity to participate in clinical research studies of new treatments. It is important to fully understand the benefits and risks of the investigational treatment.

BASIC STAGING OF COLORECTAL CANCER		
Stage	Meaning	Treatment Protocol
stage 0	cancer is in its earliest stages, completely confined to the polyp; also called CARCINOMA in situ or intramucosal carcinoma	surgery to remove the cancerous polyp (polypectomy), typically via COLONOSCOPY
stage 1	cancer involves but remains confined to the inner layers of the intestinal mucosa	surgery to remove the tumor and the involved segment of colon (local excision)
stage 2	cancer extends beyond the wall of the COLON but not into the LYMPH NODES	surgery to remove the tumor and involved segment of colon; occasionally RADIATION THERAPY or CHEMOTHERAPY
stage 3	cancer extends beyond the wall of the colon and into nearby lymph nodes	surgery to remove the tumor, the involved segment of colon, the surrounding tissue into which the cancer has spread, and the involved lymph nodes; radiation therapy or chemotherapy
stage 4	cancer has spread to other organs	surgery to remove tumors and involved tissues when possible; radiation therapy and/or chemotherapy
recurrent	a return of the cancer to the colon	surgery to remove the tumor and involved segment of colon; radiation therapy and/or chemotherapy

30 The Gastrointestinal System

Treatments for cancer offer varying benefits and risks. Cancer experts often recommend obtaining a second opinion evaluation from another physician specialist before making treatment decisions. Treatment is highly successful for colorectal cancers detected before they spread beyond the wall of the bowel. Stage 0 colorectal cancer is nearly always curable, and more than 90 percent of people diagnosed with stage 1 colorectal cancer are cancer-free five years after treatment. The course of advanced

and recurrent colorectal cancer is more challenging, and often results in moderate to significant lifestyle changes. Recovery from extensive surgery may take several months, and radiation therapy and chemotherapy typically cause numerous and varied side effects that often limit participation in regular activities. Though the outlook for colorectal cancer continues to improve with early detection and new treatment technologies, it remains a serious health condition that requires appropriate and

COLORECTAL CANCER SCREENING PROCEDURES			
Procedure	Frequency	Benefits	Drawbacks or Risks
DIGITAL RECTAL EXAMINATION (DRE)	annually after age 45	can detect growths and abnormalities in the RECTUM	does not detect very small growths or growths beyond the rectum further procedures required to investigate positive results
FECAL OCCULT BLOOD TEST (FOBT)	annually after age 50	detects microscopic blood in the stool, often while the growth causing the bleeding is still very small; sample collected at home; home-testing kits available	the growth is large enough to cause bleeding by the time of detection compliance is low further procedures required to investigate positive results
sigmoidoscopy	every 5 years for those with average risk; every 3 years for those with increased risk	provides direct examination of the walls of the rectum and sigmoid COLON; doctor can remove or biopsy detected polyps or tumors	does not visualize full length of the colon unpleasant preparation some discomfort during the procedure minimal risk of INFECTION, bleeding, or perforation further procedures required to investigate positive results
double-contrast BARIUM ENEMA	every 10 years for those with average risk; every 5 years for those with increased risk	provides clear representation of the full colon	does not detect very small polyps or tumors less effective in detecting polyps or tumors in the rectum than in the colon unpleasant preparation some discomfort during the procedure further procedures required to investigate positive results
COLONOSCOPY	every 10 years for those with average risk; every 5 years for those with increased risk	allows direct examination of the full colon; doctor can remove or biopsy detected polyps or tumors	unpleasant preparation some discomfort during the procedure requires general sedation minimal risk of infection, bleeding, or perforation

diligent attention. Cancer SUPPORT GROUPS provide excellent opportunities to share experiences and feelings in a protected setting.

Risk Factors and Preventive Measures

The most significant risk factor for colorectal cancer, as for many kinds of cancer, is age. Doctors diagnose more than 90 percent of colorectal cancer in people who are age 50 and older. Health and medical factors that present increased risk include

- of early-onset (before age 50) colorectal cancer among first-degree family members, notably parents and siblings
- previous diagnosis of colorectal cancer
- previous diagnosis of BREAST CANCER, endometrial (uterine) cancer, or OVARIAN CANCER in women
- mutations of the adenomatous polyposis coli (APC) gene, which causes FAMILIAL ADENOMATOUS POLYPOSIS (FAP), or of the gene that causes HEREDITARY NONPOLYPOSIS COLORECTAL CANCER (HNPCC); both mutations are rare, together accounting for less than 3 percent of colorectal cancers
- INFLAMMATORY BOWEL DISEASE (IBD), which may feature Crohn's disease, ulcerative COLITIS, or both
- OBESITY, notably ABDOMINAL ADIPOSITY (excess body fat carried around the belly)

Lifestyle factors that appear to increase the risk for colorectal cancer include a diet high in saturated fats (animal-based fats) and low in fruits and vegetables, lack of daily physical exercise, and smoking.

Regular screening is the most effective preventive measure for colorectal cancer. Cancer experts recommend colonoscopy as the first line of screening for colorectal cancer in most people starting at age 50, though earlier in people with family members who have had colorectal cancer at an earlier age, every 10 years for people with average risk and every 5 years for people with additional risk factors. Research suggests such screening could eliminate 80 to 90 percent of colorectal cancer.

Though conclusive evidence of dietary correlations to risk for intestinal polyps and colorectal

cancer remains elusive, cancer experts encourage a diet high in natural fiber (especially fresh fruits and vegetables) and low in saturated fat. Other lifestyle recommendations include daily physical exercise, SMOKING CESSATION, and weight management.

See also ADENOMA-TO-CARCINOMA TRANSITION; CANCER PREVENTION; CANCER RISK FACTORS; CANCER TREATMENT OPTIONS AND DECISIONS; DIET AND HEALTH; END OF LIFE CONCERNS; FIBER AND GASTROINTESTINAL HEALTH; INTESTINAL POLYP; SMOKING AND HEALTH; SURGERY BENEFIT AND RISK ASSESSMENT; WEIGHT LOSS AND WEIGHT MANAGEMENT.

colostomy A surgically created opening (stoma) through the abdominal wall through which the COLON passes fecal matter, typically accompanying surgery to remove a diseased segment of the colon. Though there are numerous medical reasons for colostomy, among the most common are COLORECTAL CANCER, traumatic injury, and severe INFLAMMATORY BOWEL DISEASE (IBD). A colostomy may be temporary when a period of nonactivity will help the colon recover from INFECTION or inflammatory damage or during the stages of reconstructive surgery. A colostomy is likely to be permanent when the surgeon must remove large segments of bowel.

The OPERATION is a major surgery done under general anesthetic. Typically the person enters the hospital the night before the scheduled OPERATION to complete the preparations for surgery, which usually include LAXATIVES and enemas to thoroughly cleanse the colon. The length of the operation depends on the extent of the procedures. The surgeon attempts to locate the colostomy in the lower abdomen when possible, though may place a temporary colostomy in the upper abdomen to rest the lower segments of the colon. Most people remain in the hospital for five to seven days, during which time an ostomy-care specialist provides education and instruction about colostomy care. HEALING after surgery takes about six to eight weeks. Diligent WOUND CARE during this period is essential to reduce the risk for infection and irritation and to help the stoma heal properly.

A small plastic bag, sealed against the SKIN with adhesive around the opening (stoma), collects fecal matter that exits the colon through the

colostomy. It is important to empty or change the colostomy bag frequently and regularly and to cleanse the skin around the stoma with each changing to minimize irritation from the adhesive and from fecal matter. Frequent bag changes also reduce odor, as do deodorizing tablets that go into the ostomy bag. Over time, most people find that certain foods (such as meats and many processed foods) are more likely than others to cause odor or irritation and can avoid eating them to further reduce odor.

Concerns about how having a colostomy will change appearance and daily living activities are natural and common. A colostomy significantly alters the body's structure and excretory function, which many people find challenging. An ostomy-care specialist can provide information and suggestions to smooth the adjustment. Most people find they are able to return to their regular activities when the stoma fully heals. The colostomy should not interfere with clothing, exercise, lifting and carrying, and most other daily activities.

The effect of colostomy on **SEXUALITY** is a major concern for most people. A risk of surgery on the colon is damage to the nerves that supply the perineal area, which can result in altered sensations in men and women and **ERECTILE DYSFUNCTION** in men. Some people feel self-conscious or embarrassed about having a colostomy. However, many people who have colostomies can return to regular sexual activity as soon as they feel the desire to do so. A special cap can cover the stoma during sex. Having **SEXUAL INTERCOURSE** or **ORGASM** does not cause any harm to the colostomy or adversely affect the underlying condition in most circumstances. It is important for partners to discuss their concerns and feelings openly and honestly so they can maintain intimacy within their relationships.

See also **ILEOANAL RESERVOIR**; **ILEOSTOMY**.

constipation Difficult or delayed bowel movements. Constipation may occur as a delay in the frequency of bowel movements, an attempt to pass stools that are hard and compact, or a combination. Constipation tends to be chronic (long-term), though can occur as acute (sudden) episodes. Abdominal cramping and bloating may accompany constipation.

Any rectal bleeding that accompanies constipation or bowel movements requires medical evaluation.

Though constipation can signal serious health conditions such as intestinal obstruction or **HYPOTHYROIDISM**, most often constipation relates to lifestyle factors such as diet, physical exercise, and **HYDRATION** (fluid intake). Numerous medications, notably **ANTIHISTAMINE MEDICATIONS**, narcotic **ANALGESIC MEDICATIONS** (pain relievers) and **ANTIDEPRESSANT MEDICATIONS**, can cause constipation. Constipation becomes more common with increasing age, partly due to lifestyle factors and partly due to age-related changes in intestinal motility.

Stools become hardened when the **COLON** extracts too much water from the fecal matter that passes through it. This can occur because the body needs more fluid (inadequate fluid intake) or because the fecal matter spends too much time in the colon (a consequence of inactivity or decreased intestinal motility). Hardened stools are difficult to pass and may cause irritation and even **ABRASIONS** to the anal canal and **ANUS**. Straining with the effort of a difficult **BOWEL MOVEMENT** aggravates common conditions such as **HEMORRHOIDS** and can have cardiovascular consequences such as **ARRHYTHMIA** (irregular heartbeat). Long-term use of **LAXATIVES** causes the colon to become reliant on them to stimulate bowel movements; overuse of laxatives is a frequent cause of chronic constipation.

For occasional constipation, many doctors recommend home treatment for two to three weeks, consisting of:

- increased water consumption
- increased fiber in the diet (eating more vegetables, fruits, whole grains, and whole grain products)
- 45 minutes to an hour of daily physical exercise such as walking, which encourages **PERISTALSIS** (the rhythmic, wavelike contractions of the intestinal wall) and improves **BLOOD** flow
- no laxatives
- sitz baths and hemorrhoidal preparations to soothe irritated hemorrhoids

These measures facilitate a return to gastrointestinal regularity for most people. Constipation that extends beyond two or three weeks, occurs with rectal bleeding, or causes ABDOMINAL PAIN or ABDOMINAL DISTENTION requires prompt medical evaluation.

See also AGING, GASTROINTESTINAL CHANGES THAT OCCUR WITH; ANAL FISSURE; DIARRHEA; FECAL IMPACTION; FECAL INCONTINENCE; FIBER AND GASTROINTESTINAL HEALTH; SITZ BATH.

Crohn's disease See INFLAMMATORY BOWEL DISEASE (IBD).

cyclic vomiting syndrome Episodes of uncontrolled VOMITING and NAUSEA, sometimes called abdominal migraine, that occur in cycles of symptoms and relief. Each episode may last hours and often repeats over a period of time after which there is an extended period without symptoms. Many people experience prodrome, a short period of time during which they have nausea, ABDOMINAL PAIN, a sense of the impending episode, or other symptoms that consistently occur before an episode. During an active episode, the person has persistent nausea and repeated vomiting that can last for hours to days.

Researchers believe the physiologic mechanisms of cyclic vomiting syndrome are similar to those of migraine headaches. Episode triggers may include infections and other physiologic stress, emotional stress, and certain foods such as chocolate. There are no conclusive diagnostic markers or tests for cyclic vomiting syndrome, making diagnosis a challenge. Generally the gastroenterologist strives to rule out other conditions that could cause the symptoms, resulting in diagnosis by exclusion.

Treatment targets symptom relief to the extent possible, which for many people is minimal, and supportive measures such as drinking plenty of fluids to replace those lost through vomiting. Some people experience relief with medications intended to head off migraine HEADACHE. Though some people can avert active episodes with medications or by altering their activities during the prodrome stage, there are no certain methods for preventing episodes. There is no known cure for cyclic vomiting syndrome, though episodes often diminish with aging. Cyclic vomiting syndrome is more common in children than adults, and can manifest in children as young as two or three years old.

See also GASTROENTERITIS.

D

diarrhea Watery or frequent bowel movements. Diarrhea can have serious health consequences for the very young, the very old, and those who have debilitating illnesses. It is important to increase fluid consumption when diarrhea is present as DEHYDRATION can occur very quickly. Diarrhea in an infant under six months old requires immediate medical attention. For older children and adults, medical attention becomes necessary when diarrhea exists with:

- ABDOMINAL PAIN for longer than two hours
- FEVER above 101°F for longer than 24 hours
- profuse VOMITING
- reduced or lack of URINATION
- suspected ingestion of toxic or obstructive substance

Bloody diarrhea may signal a serious health condition and requires immediate medical evaluation.

Numerous causes exist for diarrhea. Foods containing table sugar (sucrose), sugars that occur in milk (lactose), fruits (fructose), and sweeteners in juices and soft drinks (sorbitol and mannitol) can cause or worsen diarrhea because they draw additional fluid into the large intestine. Viral, bacterial, and parasitic infections, often food-borne, are common causes of diarrhea. Diarrhea is also a common symptom with gastrointestinal disorders such as IRRITABLE BOWEL SYNDROME (IBS) and INFLAMMATORY BOWEL DISEASE (IBD). Extended periods (weeks to months) of loose or frequent bowel movements may suggest dysfunction of the SMALL INTESTINE OR MALABSORPTION disorders. Frequent, small bowel movements that are a change from usual bowel

patterns may indicate conditions of the large intestine such as intestinal polyps or COLORECTAL CANCER. Women may have mild diarrhea with their menstrual periods. Diarrhea may occur with changes in eating habits, such as when traveling.

COMMON CAUSES OF DIARRHEA	
antibiotic therapy	CELIAC DISEASE
changes in EATING HABITS	COLORECTAL CANCER
DIVERTICULAR DISEASE	excessive ALCOHOL consumption
excessive CAFFEINE consumption	FOOD-BORNE ILLNESSES
foods and beverages	GALLBLADDER DISEASE
ILEUS	INFLAMMATORY BOWEL DISEASE (IBD)
ingested toxins	INTESTINAL POLYP
IRRITABLE BOWEL SYNDROME (IBS)	MALABSORPTION
medication SIDE EFFECTS	viral, bacterial, and parasitic INFECTION

Bland foods such as cooked rice, oatmeal, soda crackers, graham crackers, and bananas can help calm the gastrointestinal tract and restore normal bowel function. Doctors often recommend an oral rehydration solution (ORS) such as Pedialyte or Rehydralyte when diarrhea persists beyond a few days in children, and for adults who show indications of dehydration or have extensive diarrhea. Doctors may recommend ANTIDIARRHEAL MEDICATIONS such as loperamide (Imodium) that slow PERISTALSIS (intestinal movement) to help control symptoms. Most diarrhea, though disruptive, represents minor and temporary gastrointestinal disturbance that fully resolves within one to three weeks.

See also COLITIS; GASTROENTERITIS; FOOD SAFETY.

digestive enzymes Specialized protein structures that help break down (hydrolyze) foods in the

MOUTH, STOMACH, and SMALL INTESTINE to assist in absorbing NUTRIENTS from foods. Gastrointestinal structures produce dozens of digestive enzymes, which they secrete in various digestive juices. Amylase in saliva, for example, breaks down carbohydrates into their sugar components. Gastric juices combine acid and protease (pepsin) to further hydrolyze foods. Numerous enzymes in the small intestine—such as lactase, cellulase, lipase, maltase—facilitate the chemical changes necessary to convert food particles to nutrient molecules the intestinal mucosa can absorb and transport into the bloodstream. Shortages of enzymes may occur, naturally or due to health conditions, that result in gastrointestinal disorders. A shortage of lactase, for example, causes LACTOSE INTOLERANCE.

See also CARBOHYDRATE INTOLERANCE; DIGESTIVE HORMONES; NUTRITIONAL SUPPLEMENTS.

digestive hormones Chemical messengers that stimulate or inhibit gastrointestinal functions. Organs and structures of the gastrointestinal system synthesize and release digestive hormones in response to chemical and physiologic changes that take place with the ingestion of food and its passage through the gastrointestinal tract. The major digestive hormones are

- gastrin, which stimulates the STOMACH to release gastric juices and begin contracting
- cholecystokinin (CCK), which stimulates the GALLBLADDER to release BILE, the PANCREAS to release digestive juices, and the stomach to slow the release of chyme (the slushy mix of food and digestive secretions) into the DUODENUM (first segment of the SMALL INTESTINE)
- secretin, which accelerates bile release from the gallbladder, stimulates the pancreas to release bicarbonates to neutralize stomach acid, and slows the release of gastric juices as chyme advances from the stomach into the duodenum
- motilin, which stimulates PERISTALSIS (contractions of the gastrointestinal tract)
- gastric inhibitory polypeptide (GIP), which stimulates the pancreas to release INSULIN, slows (inhibits) the release of gastric juices, and slows stomach contractions
- enterogastrone, which stimulates the stomach to release chyme into the duodenum
- vasoactive intestinal peptide (VIP), which stops the production of gastric acid
- SOMATOSTATIN, which stops the release of insulin and further slows gastric motility (the stomach's contractions)

See also DIABETES; DIGESTIVE ENZYMES; HORMONE.

digital rectal examination (DRE) Direct palpation of the RECTUM in which the doctor inserts a gloved and lubricated finger into the rectum via the ANUS. DRE allows the doctor to feel for abnormal growths within the rectum and, in men, to palpate the PROSTATE GLAND for enlargement and possibly nodules that could suggest PROSTATE CANCER. The doctor can perform DRE as an office procedure; there is little discomfort. The person may lie on his or her side with knees drawn up. DRE may accompany a PELVIC EXAMINATION for a woman. DRE is also part of the examination to determine the cause of acute ABDOMINAL PAIN and other symptoms of health conditions affecting the lower gastrointestinal tract.

See also BENIGN PROSTATIC HYPERPLASIA (BPH); CANCER PREVENTION.

diverticular disease A chronic condition in which pockets of the gastrointestinal mucosa (inner lining of the intestines) bulge through weakened areas of the intestinal wall, forming HERNIA-like protrusions called diverticula. Diverticula may form anywhere along the gastrointestinal tract from the ESOPHAGUS to the RECTUM, though are most common in the sigmoid COLON. Most diverticular disease develops over decades and manifests symptoms after age 60. A congenital form of diverticular disease, Meckel's diverticulum, affects the SMALL INTESTINE, typically the ILEUM. Meckel's diverticulum is uncommon. Diverticulosis is the presence of multiple diverticula; diverticulitis occurs when diverticula become inflamed or infected. Doctors suspect diverticular disease results from changes in the gastrointestinal system that occur with aging. Though for some people the condition is debilitating, many people who have diverticular disease have few symp-

toms. Diverticular disease tends to have a more intense course in people who are under age 50 at the time of diagnosis.

Symptoms and Diagnostic Path

Diverticulosis often presents mild and vague symptoms such as intermittent lower abdominal discomfort or shows up incidentally on diagnostic testing for other reasons. Large or multiple diverticula may cause intestinal bleeding that may appear as darkened stools or obvious bleeding with bowel movements. Localized PAIN, especially REBOUND TENDERNESS, and FEVER suggest diverticulitis though also are symptoms of APPENDICITIS.

The diagnostic path may include DIGITAL RECTAL EXAMINATION (DRE), FECAL OCCULT BLOOD TEST (FOBT) to check for microscopic bleeding, abdominal X-ray, BARIUM ENEMA, and sigmoidoscopy or COLONOSCOPY. These procedures help distinguish between diverticulitis and appendicitis though sometimes the distinction is difficult. Diverticula often are apparent though barium enema and either sigmoidoscopy or colonoscopy provides definitive diagnosis. Occasionally the doctor may request COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) to obtain detailed information on the extent of the condition or to identify a surgical emergency such as ABSCESS or PERITONITIS.

SYMPTOMS OF DIVERTICULAR DISEASE

Diverticulosis	Diverticulitis
painless rectal bleeding	pronounced and localized ABDOMINAL PAIN ABDOMINAL DISTENTION or rigidity FEVER

Treatment Options and Outlook

Diverticulitis requires treatment with ANTIBIOTIC MEDICATIONS to eradicate the INFECTION and calm the INFLAMMATION. Oral antibiotics successfully treat many people; widespread or deep infection may require intravenous antibiotics or even surgical intervention to drain the infection and remove any portions of damaged bowel. Untreated diverticulitis can result in abscess or peritonitis, which are life-threatening complications. Other complications include intestinal obstructions and fistulas

(areas where the bowel erodes and establishes an opening into another structure such as the BLADDER or the VAGINA. These complications require surgical repair; a complete intestinal obstruction is an emergency.

Diverticulosis with no symptoms does not require treatment. Because diverticulosis is so prevalent among people age 50 and older, many gastroenterologists consider it nonpathologic (not a threat to health). Dietary measures such as increased fiber consumption may be enough to relieve mild symptoms such as occasional abdominal discomfort. It is important to determine the source of any intestinal bleeding, and to undergo regular COLORECTAL CANCER screening such as FOBT, sigmoidoscopy, or COLONOSCOPY. The gastroenterologist should evaluate any changes in bowel habits, persistent abdominal distention, or other circumstances that could suggest a different diagnosis.

Risk Factors and Preventive Measures

The primary risk factor for diverticulosis appears to be aging. Doctors commonly detect diverticula that do not cause symptoms in people who have gastrointestinal imaging procedures done for other reasons. People who are aware they have diverticulosis should try to maintain eating habits that support good gastrointestinal health, making sure they consume enough dietary fiber and water.

See also AGING, GASTROINTESTINAL CHANGES THAT OCCUR WITH; BOWEL MOVEMENT; GASTROINTESTINAL BLEEDING; ILEUS; PELVIC INFLAMMATORY DISEASE (PID); PROCTITIS.

duodenum The first segment of the SMALL INTESTINE, which receives partially digested and liquefied food (called chyme) from the STOMACH. The common BILE duct ends in the duodenum, channeling bile from the GALLBLADDER to the small intestine. Much of the activity of digestion takes place in the duodenum, where an abundance of DIGESTIVE ENZYMES combines with the bile to further break down food particles into their core nutrient molecules. Digestive content that leaves the duodenum for its journey through the remainder of the intestinal tract is almost watery because of the added digestive fluids. The remaining segments of the small intestine, the ILEUM and the JEJUNUM,

absorb the nutrient molecules that result from the duodenum's activity. The duodenum is the most common site of the ulcers that characterize PEPTIC ULCER DISEASE.

For further discussion of the duodenum and the small intestine within the context of gastrointestinal structure and function, please see the overview section "The Gastrointestinal System."

See also [BILE DUCTS](#); [LIVER](#); [PANCREAS](#).

dyspepsia The clinical term for indigestion or heartburn. Most people experience dyspepsia as a burning PAIN in the upper abdomen. Some people also experience NAUSEA, VOMITING, and excessive belching. Certain foods or drinks, such as spicy foods or caffeinated beverages, often worsen the discomfort, as do medications such as aspirin and other NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) and numerous prescription medications. ANTACIDS sometimes bring temporary relief. PEPTIC

ULCER DISEASE and GASTROESOPHAGEAL REFLUX DISORDER (GERD) are common causes of dyspepsia. Rarely, persistent dyspepsia indicates STOMACH CANCER.

The diagnostic path may include upper endoscopy, esophagogastroduodenoscopy (EGD) (examination of the ESOPHAGUS, STOMACH, and DUODENUM with a lighted, flexible tube), or BARIUM SWALLOW to rule out other causes of the symptoms. Treatment targets the underlying cause and usually includes a medication to suppress gastric acid production, such as H2 ANTAGONIST (BLOCKER) MEDICATIONS OR PROTON PUMP INHIBITOR (PPI) MEDICATIONS. The doctor may also prescribe an ANTIBIOTIC MEDICATIONS to eradicate *HELICOBACTER PYLORI* BACTERIA, the typical cause of gastric and duodenal ulcers, when the underlying condition is peptic ulcer disease. Most dyspepsia dramatically improves within six to eight weeks of appropriate treatment.

See also [ACHALASIA](#); [BARRETT'S ESOPHAGUS](#); [ENDOSCOPY](#); [GALLBLADDER DISEASE](#); [GASTRITIS](#).



endoscopic retrograde cholangiopancreatography (ERCP) An endoscopic procedure that allows diagnostic as well as therapeutic procedures involving the DUODENUM, pancreatic duct, and common BILE duct. After administering a sedative the gastroenterologist inserts the flexible, lighted endoscope through the MOUTH, passing it down the ESOPHAGUS and through the STOMACH to the duodenum. While advancing the endoscope the gastroenterologist examines these structures. Once the endoscope is in the duodenum, the gastroenterologist inserts a catheter through the ampulla of Vater and injects contrast into the common bile duct, pancreatic duct, and right and left intrahepatic ducts. X-rays taken after the injection of radiopaque dye into the ducts can show blockages and narrowing of the ducts. Through ERCP the gastroenterologist can take tissue samples for biopsy, remove small gallstones, and perform other treatments. ERCP takes about an hour, after which the person rests in a recovery area for

another two to three hours until the sedative wears off. ERCP has few risks and can help a person avoid more invasive surgery.

See also [BILE DUCTS](#); [ENDOSCOPY](#); [PANCREAS](#); [PANCREATITIS](#); [SURGERY BENEFIT AND RISK ASSESSMENT](#).

endoscopy The collective term for minimally invasive procedures that allow the doctor to view internal organs and structures using a lighted, flexible scope inserted through a natural body opening or through a small incision. Endoscopy can be diagnostic or therapeutic. Most endoscopic procedures require preparation before the procedure, sedation during the procedure, and supervised recovery after the procedure.

The primary risks of endoscopic procedures are minimal, consisting of primarily INFECTION or bleeding that results from unintended ABRASIONS to the tissues. A very rare but serious complication of endoscopic procedures of the bowel is perforation, in which the endoscope goes through the wall of

COMMON GASTROINTESTINAL ENDOSCOPY PROCEDURES

Procedure	Description and Purpose	Preparation
anoscopy	short, rigid scope for viewing the anal canal inserted through the ANUS diagnose HEMORRHOIDS, ANAL FISSURE, anal polyps, INFECTION	bowel evacuation (LAXATIVES OR ENEMA before the procedure)
colonoscopy	flexible scope with a camera for viewing the full length of the COLON inserted through the anus detect and remove INTESTINAL POLYP diagnose inflammatory or infectious conditions evaluate bleeding or possible ILEUS (intestinal obstruction) biopsy suspicious growths or tumors	multiday bowel preparation, including dietary restrictions and a potent laxative to completely clear the colon intravenous sedation and pain medication during procedure

Procedure	Description and Purpose	Preparation
esophagoscopy	flexible scope with a camera for viewing the ESOPHAGUS inserted through the mouth diagnose esophagitis, BARRETT'S ESOPHAGUS, ESOPHAGEAL ATRESIA, HIATAL HERNIA, and ESOPHAGEAL CANCER evaluate SWALLOWING DISORDERS	fasting for 6 to 12 hours before the procedure intravenous sedation and pain medication during the procedure
esophagogastroduodenoscopy (EGD)	flexible scope with a camera for viewing the esophagus, stomach, and DUODENUM inserted through the mouth diagnose esophageal conditions, PEPTIC ULCER DISEASE evaluate upper GASTROINTESTINAL BLEEDING or PAIN, swallowing difficulties, or INFLAMMATION	fasting for 6 to 12 hours before the procedure intravenous sedation and pain medication during the procedure
gastrosocopy	flexible scope with a camera for viewing the stomach inserted through the mouth take tissue samples to determine whether <i>HELICOBACTER PYLORI</i> is present cauterize bleeding ulcer	fasting for 6 to 12 hours before the procedure intravenous sedation and pain medication during the procedure
laparoscopy	flexible scope with a camera for viewing the structures of the internal abdominal cavity inserted through a small incision in the abdominal wall diagnose and treat numerous conditions (PERITONITIS, HEPATIC ABSCESS, diverticular disease, CELIAC DISEASE, gallstones, GALLBLADDER DISEASE, APPENDICITIS, PELVIC INFLAMMATORY DISEASE [PID]) numerous surgical procedures (APPECTECTOMY, CHOLECYSTECTOMY, HERNIA repair)	fasting for 6 to 12 hours before the procedure possible bowel cleansing (laxatives and enema) intravenous sedation and pain medication, epidural anesthetic, or general anesthetic
sigmoidoscopy	rigid scope or flexible scope with a camera for viewing the rectum and sigmoid colon inserted through the anus diagnose inflammation, infection, rectal polyps, rectal prolapse biopsy suspicious growths evaluate lower gastrointestinal tract bleeding	bowel evacuation (laxative or enema before the procedure)

the bowel. This requires surgical repair and ANTIBIOTIC MEDICATIONS to prevent PERITONITIS. Most people return to full and regular activities the day after diagnostic endoscopy and within a few weeks after endoscopic operations.

See also ANTIBIOTIC PROPHYLAXIS; ARTHROSCOPY; BRONCHOSCOPY; CANCER PREVENTION; CYSTOSCOPY; MINIMALLY INVASIVE SURGERY; SURGERY BENEFIT AND RISK ASSESSMENT.

enema The instillation of fluid into the RECTUM through the ANUS to stimulate a BOWEL MOVEMENT. An enema may relieve CONSTIPATION or be part of the preparation to cleanse the COLON for diagnostic procedures or surgery. Frequent enemas may result in dependence on them for bowel movements. Eating a diet high in fiber helps promote healthy bowel motility to prevent constipation. Doctors sometimes prescribe enemas containing hydrocortisone (a corticosteroid medication) to treat ulcerative COLITIS, a form of INFLAMMATORY BOWEL DISEASE (IBD), to deliver the medication directly to the sites of INFLAMMATION.

See also CORTICOSTEROID MEDICATIONS; LAXATIVES.

enteritis See GASTROENTERITIS.

esophageal atresia A CONGENITAL ANOMALY in which the ESOPHAGUS fails to form properly and does not connect to the STOMACH. The esophagus may stop short at any location from the back of the THROAT to the top of the stomach or may extend to the stomach but not connect. Often there is also a tracheal–esophageal fistula (opening between the TRACHEA and the esophagus) that allows excessive air to enter the stomach and can permit saliva as well as gastric secretions to enter the LUNGS. These anomalies require emergency intervention. The risk of ASPIRATION is especially serious, as fluids in the lungs can quickly lead to INFECTION and PNEUMONIA.

Treatment requires surgery, the nature and timing of which depend on where the esophagus ends. The doctor may surgically insert a feeding tube into the stomach to instill breast milk or formula for feeding, as well as a nasogastric tube into the portion of esophagus extending from the throat to suction saliva. Because the esophagus elongates as the child grows, doctors sometimes

delay complete surgical reconstruction for 6 to 18 months. The feeding and suction tubes remain in place until the surgery, sometimes a series of operations over several months, is complete.

The esophagus forms very early in PREGNANCY, at about 30 gestational days. Nearly always esophageal atresia and any related anomalies show up on prenatal ULTRASOUND so both doctors and parents can make treatment decisions before the infant's birth. Esophageal atresia tends to occur as one of numerous congenital anomalies that may involve the spine, HEART, other parts of the gastrointestinal system, the kidneys, and the extremities, a constellation doctors refer to as VACTERL. Doctors often use MAGNETIC RESONANCE IMAGING (MRI) or COMPUTED TOMOGRAPHY (CT) SCAN to thoroughly examine the infant for these anomalies.

See also ANAL ATRESIA; BIRTH DEFECTS; BOWEL ATRESIA; CONGENITAL HEART DISEASE; VACTERL.

esophageal cancer Malignant growths in the ESOPHAGUS. CANCER of the esophagus takes one of two forms: ADENOCARCINOMA or squamous cell CARCINOMA. Adenocarcinoma is the more common form and nearly always originates near the esophageal entry to the STOMACH. Esophageal adenocarcinoma is nearly always a progression of BARRETT'S ESOPHAGUS, a condition in which the tissue structure of the esophagus changes to resemble that of the intestines. Adenocarcinoma can develop only in this altered tissue. Squamous cell carcinoma can develop anywhere along the esophagus and is more common in people who smoke. However, smoking, particularly in combination with excessive ALCOHOL consumption, is a major risk factor for either form of esophageal cancer. People who have untreated GASTROESOPHAGEAL REFLUX DISORDER (GERD) or ACHALASIA also face increased risk, as these conditions expose the esophagus to repeated irritation and INFLAMMATION. Though five-year survival rates have increased fourfold since the 1960s, esophageal cancer remains among the most deadly cancers because it shows few symptoms until the cancer is quite advanced.

Symptoms and Diagnostic Path

The most common symptom is difficulty swallowing (dysphagia), particularly the sensation of food

getting stuck when swallowing. Other symptoms include unintentional weight loss and sensations that are a combination of pressure and **DYSPEPSIA** (heartburn). Unfortunately these symptoms are vague enough that many people can ignore them or perceive them as insignificant, allowing the cancer to progress undetected.

The diagnostic path may include **BARIUM SWALLOW**, a series of X-rays to visualize the upper gastrointestinal tract, and **ENDOSCOPY**, in which the gastroenterologist directly views the esophagus using a flexible, lighted scope. Endoscopy allows biopsy of suspicious tissue. Procedures to help determine how far the cancer has spread include endoscopic **ULTRASOUND**, **COMPUTED TOMOGRAPHY (CT) SCAN**, **MAGNETIC RESONANCE IMAGING (MRI)**, and **POSITRON EMISSION TOMOGRAPHY (PET) SCAN**.

Treatment Options and Outlook

The findings of the diagnostic procedures determine treatment options, which include

- Surgery to remove the cancerous portion of the esophagus and nearby tissue; this treatment is most effective when the cancer remains confined to the area of the esophagus where it originated. The surgeon then pulls the stomach up to connect it to the shortened esophagus, or uses a segment of intestine (called a graft) to construct a replacement for the removed section.
- **RADIATION THERAPY** to kill the cancerous cells; this treatment typically shrinks but does not eliminate the cancer, providing relief from swallowing difficulties.
- **CHEMOTHERAPY** attacks cancer cells throughout the body; this treatment is most effective when the cancer has spread to other locations in the body.

Treatment often combines these approaches. Each approach has significant risks and side effects. As with all cancers, early detection significantly improves the effectiveness of treatment.

Risk Factors and Preventive Measures

The key risk factors for esophageal cancer are Barrett's esophagus and a combination of smoking and excessive alcohol consumption. Preventive

measures to reduce the risk factors for esophageal cancer include

- **SMOKING CESSATION**
- moderation in **ALCOHOL** consumption
- **WEIGHT LOSS AND WEIGHT MANAGEMENT**
- management of chronic conditions that irritate the esophagus, notably **GERD**
- regular esophageal endoscopy for people who have Barrett's esophagus

See also **ADENOMA-TO-CARCINOMA TRANSITION**; **CANCER PREVENTION**; **CANCER RISK FACTORS**; **CANCER PREVENTION**; **CANCER TREATMENT OPTIONS AND DECISIONS**; **SMOKING AND HEALTH**; **STAGING AND GRADING OF CANCER**.

esophageal spasm Nonfunctional and often painful contractions of the muscles that line the wall of the **ESOPHAGUS**. The main symptom of esophageal **SPASM** is difficult and painful swallowing. The spasms may involve only one portion of the esophagus or the entire length of the esophagus. Doctors do not know what causes esophageal spasm, though eating foods or drinking beverages that are extremely hot or extremely cold often triggers a spasm. The diagnostic path often includes manometry, a procedure that measures pressures within the esophagus. Treatment options include medications to relax smooth muscle such as nitrates and calcium channel antagonist (blocker) medications. **BOTULINUM THERAPY**, in which botulinum toxin injected into portions of the esophagus to paralyze it, relieves symptoms in many people.

See also **ESOPHAGITIS**.

esophageal varices Enlarged and weakened veins in the walls of the **ESOPHAGUS**. Esophageal varices result from **PORTAL HYPERTENSION**, a condition of impaired **BLOOD** flow into the **LIVER**, and are potentially life-threatening should they rupture and **HEMORRHAGE**. Portal hypertension is a common complication of conditions such as **CIRRHOSIS** and chronic **HEPATITIS** that cause **SCAR** tissue to develop within the liver. Symptoms include **GASTROINTESTINAL BLEEDING** (**VOMITING** blood or passing blood in the stool), thirst that increased fluid consumption does not quench, lightheadedness, and mental

confusion (hepatic ENCEPHALOPATHY) resulting from toxins the damaged liver can no longer filter from the blood.

ENDOSCOPY (in which the gastroenterologist passes a lighted, flexible scope into the upper gastrointestinal tract) is the primary diagnostic procedure, allowing the gastroenterologist to see the ESOPHAGUS, STOMACH, and DUODENUM (first segment of the SMALL INTESTINE). The endoscopy reveals the swollen veins, which the gastroenterologist can ligate (band or tie off) or inject with a DRUG to clot the blood inside the VEIN. Bleeding esophageal varices require emergency treatment, nearly always endoscopic treatment to stop the bleeding. A radiologist can do an interventional procedure called TIPPS (transjugular intrahepatic portosystemic shunt) to decrease portal pressure and stop variceal bleeding. When other efforts are not successful a surgeon may place a shunt (tube that reroutes the flow of blood) to improve blood flow into the liver, relieving the pressure blood encounters when trying to enter the liver. Usually the end treatment for esophageal varices is LIVER TRANSPLANTATION.

See also HYPOTENSION; LIVER FAILURE.

esophagitis INFLAMMATION of the ESOPHAGUS. The most common cause of esophagitis is irritation from STOMACH contents that backflow into the esophagus, such as occurs with GASTROESOPHAGEAL REFLUX DISORDER (GERD) and ACHALASIA. INFECTION resulting from HERPES SIMPLEX, CYTOMEGALOVIRUS (CMV), or yeast (*Candida*) also can involve the esophagus to cause esophagitis. Symptoms include painful or difficult swallowing and DYSPEPSIA. The diagnostic path may include ENDOSCOPY to examine, biopsy, or culture the esophagus. Treatment

targets the underlying cause and may include H2 ANTAGONIST (BLOCKER) MEDICATIONS OR PROTON PUMP INHIBITOR MEDICATIONS to reduce the volume of gastric acid. ANTIBIOTIC MEDICATIONS OR ANTIFUNGAL MEDICATIONS are necessary to treat INFECTION. Most people fully recover when the underlying condition resolves, though often esophagitis becomes chronic.

See also BARRETT’S ESOPHAGUS; GASTRITIS; GASTROENTERITIS; SWALLOWING DISORDERS.

esophagus The muscular tube that extends from the back of the THROAT to the top of the STOMACH. From 10 to 12 inches long, the esophagus carries ingested food and fluids to the stomach to begin the process of digestion. As the esophagus leaves the throat its MUSCLE tissue is primarily striated (voluntary); as the esophagus enters the stomach its muscle tissue is smooth (involuntary). Though a person can control the initiation of swallowing, the processes that propel food down the esophagus and into the stomach are involuntary.

COMMON CONDITIONS AFFECTING THE ESOPHAGUS	
ACHALASIA	BARRETT’S ESOPHAGUS
DIVERTICULAR DISEASE	DYSPEPSIA
ESOPHAGEAL ATRESIA	ESOPHAGEAL CANCER
ESOPHAGEAL SPASM	ESOPHAGEAL VARICES
ESOPHAGITIS	GASTROESOPHAGEAL REFLUX DISORDER (GERD)

For further discussion of the esophagus within the context of gastrointestinal structure and function, please see the overview section “The Gastrointestinal System.”

See also ANUS; CECUM; COLON; DUODENUM; ILEUM; JEJUNUM; RECTUM.

familial adenomatous polyposis (FAP) A genetic disorder in which hundreds of intestinal polyps grow in the RECTUM and COLON. FAP is an extreme risk for early-onset COLORECTAL CANCER. This autosomal dominant disorder results from a defective gene, inherited from one parent, in which there is a MUTATION of the adenomatous polyposis coli (APC) GENE. The ACP gene regulates the proteins that inhibit adenomas (abnormal growths arising from epithelial cells, the cells that form the surface layer of SKIN and membranes) in the intestinal mucosa. The mutation of the ACP gene blocks these proteins, allowing adenomas, called intestinal polyps when they occur in the colon, to flourish. In FAP polyps are generally abundant by late ADOLESCENCE, with COLORECTAL CANCER developing before age 40.

The rapid and prolific growth of FAP-associated intestinal polyps significantly favors their evolution to malignancies, manifesting primarily as colorectal adenocarcinomas though may also occur in other sections of the gastrointestinal tract, notably the DUODENUM. FAP polyps and malignancies seldom show early symptoms; family history is the most important diagnostic factor. Signs of FAP include specific dental anomalies and retinal changes that are apparent in childhood. CANCER experts recommend screening COLONOSCOPY annually beginning in early adolescence, and every three to six months when polyp growth becomes pronounced.

Colonoscopy allows the gastroenterologist to remove large intestinal polyps and polyps showing DYSPLASIA (cellular changes indicating that ADENOMA-TO-ADENOCARCINOMA TRANSITION is under way). Studies suggest some NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) may slow the growth of adenomas, reducing the number and size of the

polyps. However, these medications do not alter the course of the disease, and surgery to remove the most heavily involved sections of intestine ultimately becomes the therapeutic solution.

Doctors often recommend prophylactic total bowel resection (removal of the colon and rectum) to eliminate the potential for colorectal cancer. Presently this is the only means to prevent FAP from developing into colorectal cancer. Advances in GENE THERAPY show the greatest potential for less invasive and more effective treatments in the future. Participation in clinical research studies that are evaluating investigational treatments may present other treatment opportunities.

See also [ADENOMA](#); CANCER PREVENTION; CANCER RISK FACTORS; CELL STRUCTURE AND FUNCTION; GENETIC DISORDERS; [HEREDITARY NONPOLYPOSIS COLORECTAL CANCER \(HNPCC\)](#); [ILEOANAL RESERVOIR](#); [ILEOSTOMY](#); INHERITANCE PATTERNS.

fatty liver See [STEATOHEPATITIS](#).

fecal impaction Hardened pieces of feces, also called stool, that lodge in the COLON OR RECTUM. Fecal impaction typically occurs as a consequence of chronic CONSTIPATION or reduced bowel motility (movement of digestive waste through the colon) and is most common in people who are confined to bed for extended periods of time. Those who take narcotic PAIN medications or ANTIDIARRHEAL MEDICATIONS may also develop fecal impaction. Symptoms may include extended time without a BOWEL MOVEMENT, lower abdominal cramping or pain, and DIARRHEA from stool leaking around the impaction. DIGITAL RECTAL EXAMINATION (DRE) allows the doctor to make the diagnosis. Treatment may include manual removal of the impaction or ENEMA to soften the impaction and stimulate

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bowel movements to expel it. Increased fiber in the diet, stool softeners (medications that help the stool retain fluid), increased fluid consumption, and daily physical activity such as walking when possible can help prevent constipation and fecal impaction.

See also DIET AND HEALTH; SPINAL CORD INJURY; TOXIC MEGACOLON.

fecal incontinence Loss of bowel control. Fecal incontinence occurs more frequently in young children and in elderly adults, though can occur at any age. FECAL IMPACTION, in which stool hardens in the RECTUM, is a common cause of fecal incontinence, particularly in children, as digestive waste that continues to move through the COLON forces its way around the impaction and leaks from the ANUS because the rectum has no capacity to store it. Fecal incontinence also may result from injury or damage to the nerves that provide sensation to the perineum and rectal area or that control the anal sphincter (MUSCLE that regulates the discharge of stool). Such injury may be congenital (such as may occur with SPINA BIFIDA and other congenital anomalies affecting the SPINAL CORD), the consequence of trauma to the perineal area during CHILDBIRTH (particularly EPISIOTOMY), a complication of surgery (such as to treat HEMORRHOIDS OR ANAL FISSURE), or a SIDE EFFECT OF RADIATION THERAPY to treat CANCER.

Though fecal incontinence is more common among those over age 70, it is not a natural consequence of aging. Treatment can improve or eliminate fecal incontinence in most circumstances. Treatment may include “retraining” the defecation response (BIOFEEDBACK), surgery to repair damaged muscle tissues or a weakened anal sphincter, or therapies to relieve INFLAMMATORY BOWEL DISEASE (IBD) and other conditions in which there is INFLAMMATION of the colon. Eating more fruits, vegetables, and whole grain products adds fiber to the diet, which improves gastrointestinal motility (the movement of digestive content through the gastrointestinal tract). Regular physical activity, such as daily walking, also improves gastrointestinal motility.

See also CONGENITAL ANOMALY; CONSTIPATION; DIARRHEA; DIVERTICULAR DISEASE; FIBER AND GASTROINTESTINAL HEALTH; RECTAL PROLAPSE.

fecal occult blood test (FOBT) A laboratory test to determine whether there is microscopic (occult) BLOOD in the stool, primarily to screen for COLORECTAL CANCER although other conditions, such as INFLAMMATORY BOWEL DISEASE (IBD) and diverticulosis, can also cause occult bleeding. Two kinds of FOBT kits are available for self-sampling at home, one that a laboratory tests and the other that shows immediate results.

For the conventional guaiac test, the person receives a kit from the doctor. The kit contains three cards onto which the person applies a small stool sample, one sample each day for three days. The cards go into a prepaid envelope for mailing to the laboratory (or may be returned to the doctor's office). The lab applies a chemical, guaiac, that reacts with heme, a component of the HEMOGLOBIN in blood. The reaction produces a blue coloration, a positive result. No color change indicates a negative result (no blood is present).

Any positive FECAL OCCULT BLOOD TEST (FOBT) result requires further medical evaluation to determine the source of the bleeding and to rule out serious conditions such as COLORECTAL CANCER.

Tests that show immediate results are available in most pharmacies and drugstores without a doctor's prescription. They contain reagent tissues that the person drops into the toilet following a BOWEL MOVEMENT (before flushing). The tissue turns blue-green if there is any heme present, indicating blood and remains colorless when no blood is present. As with the conventional test, the person tests three bowel movements over three days. The kit includes a card that the person can fill out and send to his or her doctor or keep for personal health records.

The FOBT is a good test for colorectal cancer because the intestinal polyps that are its starting points bleed easily, though the bleeding often is not apparent with visual examination of the stool. Many health conditions can cause positive results, such as ulcers, DIVERTICULAR DISEASE, HEMORRHOIDS, and ANAL FISSURE. Certain foods and other substances can cause false-positive or false-negative results with guaiac-based tests; test instructions may advise avoiding them for 48 hours before

performing the tests (seven days for aspirin and NONSTEROIDAL ANTI-INFLAMMATORY DRUGS [NSAIDS]). Women should do FOBT when they are not menstruating.

SUBSTANCES THAT MAY ALTER FOBT RESULTS	
False-Positive Results	False-Negative Results
red meat	vitamin C supplements
cruciferous vegetables	citrus fruits and juices
cantaloupe	

Health-care professionals recommend FBOT annually starting at age 45 for both men and women as a screening for colorectal cancer. Doctors also may request FBOT when they suspect conditions that can cause GASTROINTESTINAL BLEEDING and when there is ANEMIA for no apparent reason.

See also CANCER PREVENTION; COLONOSCOPY.

fiber and gastrointestinal health Fiber, the indigestible residue of plant-based foods, adds bulk to the gastrointestinal contents. This bulk helps stimulate PERISTALSIS, the rhythmic MUSCLE contractions of the intestinal wall that move gastrointestinal contents through the digestive process. In the SMALL INTESTINE where digestive juices work to break down food particles into molecules of NUTRIENTS, the consistency fiber adds to the chyme (the thick, liquid mixture the STOMACH sends to the intestines) helps keep the food in the small intestine long enough for complete digestion to take place. In the COLON, fiber helps maintain more fluid in the stool, keeping this digestive waste soft enough to pass easily from the body during a BOWEL MOVEMENT.

A number of studies suggest a diet high in fiber and low in saturated fats measurably reduces the risk for intestinal polyps as well as for COLORECTAL

CANCER. Good sources of dietary fiber include fruits, vegetables, and whole grains and whole grain products. Products such as methylcellulose (Citrucel) and psyllium (Metamucil) can supplement dietary fiber. Drinking plenty of water is also important to keep the body hydrated, which reduces the amount of water the colon extracts from digestive waste.

See also CONSTIPATION; DIARRHEA; INTESTINAL POLYP; NUTRITIONAL NEEDS.

flatulence The clinical term for intestinal gas. Flatulence indicates undigested food particles are present in the COLON. Consuming large quantities of indigestible fiber (such as with beans and other legumes), eating too fast to thoroughly chew food before swallowing, and eating a larger quantity of food than the gastrointestinal tract can accommodate are common reasons for excessive amounts of undigested food particles to make it to the colon. BACTERIA naturally present in the colon act on these food particles. In addition to breaking them down into nutrient molecules, the bacteria also produce gas as a byproduct. These gases eventually make their way through the colon and escape through the ANUS. The most common of these are methane and hydrogen sulfide, which give flatulence its characteristic odor. Excessive flatulence often causes lower abdominal discomfort and cramping. It may occur with LACTOSE INTOLERANCE, CARBOHYDRATE INTOLERANCE, and MALABSORPTION and as a SIDE EFFECT of numerous medications. The herbs peppermint, GINGER, and CHAMOMILE reduce intestinal gas, as do products containing simethicone, activated charcoal, or enzymes that help break down cellulose (residual fiber).

See also ANTACIDS.



gallbladder A small, muscular pouch on the underside of the LIVER that concentrates and stores BILE. The gallbladder absorbs about 90 percent of the water in the bile that arrives from the liver, creating concentrated, potent bile. Fats and proteins in the chyme (partly digested food) the STOMACH sends to the DUODENUM trigger the duodenum to release the digestive HORMONE cholecystokinin (CCK). CCK stimulates the gallbladder to contract, expelling bile into the duodenum to aid with digestion. The most common health conditions that affect the gallbladder are cholelithiasis (gallstones), cholecystitis (INFLAMMATION of the gallbladder), and biliary dyskinesia (inadequate contraction of the gallbladder). CANCER of the gallbladder occurs though is rare.

For further discussion of the gallbladder within the context of gastrointestinal structure and function, please see the overview section “The Gastrointestinal System.”

See also [CHOLECYSTECTOMY](#); [DIGESTIVE HORMONES](#); [GALLBLADDER DISEASE](#).

gallbladder disease Disorders and dysfunctions of the GALLBLADDER. Gallbladder disease becomes more common with increasing age. Though medical treatments can help some people with gallbladder disease, surgery to remove the gallbladder is the most common treatment and permanently resolves symptoms in about 90 percent of people who have primary gallbladder disease. Tumors and CANCER of the gallbladder occur, though are very rare. INFLAMMATION of the BILE DUCTS and HEPATITIS also can affect BILE production and gallbladder function. Gallbladder disease can be acute or chronic.

Biliary dyskinesia Dysfunction of the gallbladder prevents it from contracting to eject bile, reducing or stopping the flow of bile from the gall-

bladder to the DUODENUM (first segment of the small intestine). Biliary dyskinesia may occur as a result of injury to the nerves that supply the gallbladder, as a consequence of metabolic disorders affecting LIVER function, or for unknown reasons (most common).

Cholelithiasis Commonly called gallstones, cholelithiasis develops over years to decades in most people. Gallstones can range in size from a few millimeters to several centimeters. There can be one to a few to dozens. About 80 percent of gallstones contain mostly cholesterol; bile pigments such as BILIRUBIN make up the remainder. Many people have gallstones without symptoms. Gallstones become a health concern when they lodge in the bile ducts or when they cause irritation and inflammation of the gallbladder's mucosal lining. In a variation of cholelithiasis, called choledocholithiasis, the gallstones form in the bile ducts.

Cholecystitis Inflammation or INFECTION of the gallbladder most commonly occurs in conjunction with gallstones that block the flow of bile out of the gallbladder, though it can develop in biliary dyskinesia when the bile in the gallbladder stagnates. This stagnation irritates and inflames the lining of the gallbladder. Cholecystitis that occurs without gallstones is acalculus cholecystitis.

GALLBLADDER DISEASE AND WEIGHT LOSS

These weight-loss efforts increase the risk for gallbladder disease:

- rapid weight loss (3 pounds a week or greater)
 - BARIATRIC SURGERY (gastric banding, stapling, bypass)
 - weight loss cycling (cycles of loss and regaining weight, especially large amounts)
-

Symptoms and Diagnostic Path

PAIN is the primary symptom of gallbladder disease, and is characteristically:

- steady, sometimes intense pain between the right rib cage and shoulder blade felt in the front, back, or both
- brought on by eating fatty foods, often occurring several hours after eating
- common at night, waking one from sleep
- one to five hours in duration
- not relieved by changing positions or taking over-the-counter pain medications

Other symptoms of gallbladder disease include NAUSEA, VOMITING, gastrointestinal distress (gas, bloating, DIARRHEA) not relieved by ANTACIDS, and light-colored stools that contain noticeable mucus. When a gallstone blocks a bile duct there often is JAUNDICE (yellowish discoloration of the SKIN) and severe tenderness over the site of the blockage. FEVER, chills, and unrelenting pain may signal an infection in the gallbladder. These circumstances require immediate medical attention.

The doctor's physical examination includes a careful history of symptoms as well as palpation of the abdomen. The diagnostic path typically includes ULTRASOUND of the upper right abdomen, which can detect gallstones as small as 2 millimeters—about the size of a thick pencil lead. It also can show thickening of the gallbladder's wall, an indication of chronic inflammation and previous gallstone development. Because the liver shadows the gallbladder, ultrasound does not always detect inflammation related to acute cholecystitis or certain other gallbladder problems. Contrast dye X-RAY (oral or intravenous) and radioisotope imaging (cholescintigraphy) provide detailed information about gallbladder function.

Treatment Options and Outlook

Mild and infrequent symptoms may require no intervention beyond watchful waiting and lifestyle modifications such as eating a diet lower in fat, getting daily physical exercise, and WEIGHT LOSS AND WEIGHT MANAGEMENT. ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) often is successful in removing small gallstones from the bile ducts.

Surgery to remove the gallbladder (CHOLECYSTECTOMY) is the treatment of choice for acute, recurrent, or chronic cholecystitis and cholelithiasis in which gallstones cause pain and bile duct obstruction. There are two methods for performing cholecystectomy: laparoscopic surgery and OPEN SURGERY. About 95 percent of cholecystectomies performed in the United States are laparoscopic.

Medications to dissolve gallstones are not very successful and can cause significant side effects. Current treatment guidelines recommend these medications only when surgery is not a viable option. The two drugs doctors sometimes use are ursodiol (Actigall) and chenodiol (Chenix). Though EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY (ESWL) is effective in breaking up KIDNEY stones, it so far has not proven to be successful in doing the same with gallstones.

About a third of people who have one gallbladder episode, such as a gallstone that causes pain, never have another. The gallbladder is an organ that, though useful, the body does not require. Most people make a full recovery from gallbladder surgery and can resume their normal activities without modification. No dietary restrictions or medications are necessary.

Risk Factors and Preventive Measures

Women are twice as likely as men to develop gallbladder disease. Researchers believe this increased risk correlates to the presence of ESTROGENS, which play an integral role in cholesterol METABOLISM. Women who are pregnant or taking oral contraceptives (birth control pills), which increase the body's level of estrogen, are at highest risk. Gallbladder disease seldom occurs in children.

These factors increase the risk for gallbladder disease in men and women alike:

- OBESITY
- rapid weight loss or weight cycling
- DIABETES
- taking lipid-lowering medications
- age 60 or older

Lifestyle habits such as nutritious diet and regular physical exercise minimize the likelihood of

gallbladder disease. Dietary fiber helps absorb cholesterol from consumed foods, reducing the amount of cholesterol that becomes available in the bloodstream and for the liver to process.

See also DIET AND HEALTH; **ENDOSCOPY**; HYPERLIPIDEMIA; LIFESTYLE AND HEALTH; MINIMALLY INVASIVE SURGERY; **PRIMARY BILIARY CIRRHOSIS**; PRIMARY SCLEROSING CHOLANGITIS.

gastrectomy Partial or complete surgical removal of the STOMACH, typically to treat STOMACH CANCER or uncontrollable bleeding resulting from PEPTIC ULCER DISEASE. Gastrectomy is a major OPERATION, typically an OPEN SURGERY, performed under general ANESTHESIA that requires several days to a week in the hospital and 8 to 12 weeks for total recovery and return to regular activities. An individual's course of recovery depends on the reasons for the surgery. The surgical operation takes two to three hours. After removing the diseased portion of the stomach through an abdominal incision at the lower edge of the left rib cage, the surgeon connects the remaining portion of the stomach (or the ESOPHAGUS, when the gastrectomy is total) to the DUODENUM. A partial (also called subtotal) gastrectomy leaves a gastric pouch that can carry on some of the digestive functions of the stomach. Total gastrectomy, which is less common, leaves no residual gastric pouch though the surgeon may construct one by expanding a portion of the duodenum.

Many people are able to return to normal eating habits after they recover from the surgery, though find that they need to eat frequent small meals to accommodate the smaller stomach and reduce gastrointestinal distress. Foods that are high in protein and low in simple sugars are easier for the small intestine to digest without the aid of the stomach. Some people have difficulty eating regular foods after gastrectomy and need to use NUTRITIONAL SUPPLEMENTS, typically liquid preparations, to meet their NUTRITIONAL NEEDS.

Risks and complications of gastrectomy include bleeding, INFECTION, dumping syndrome (RAPID GASTRIC EMPTYING), and damage to the vagus NERVE (which regulates gastric PERISTALSIS and other digestive functions). People who have total gastrectomies, and many people who have subtotal gastrectomies, need regular injections of vitamin

B₁₂ (cyanocobalamin) because the gastric mucosa is no longer able to produce intrinsic factor, a chemical substance that allows the SMALL INTESTINE to absorb this vital nutrient. Vitamin B₁₂ deficiency causes pernicious ANEMIA.

See also BARIATRIC SURGERY; CANCER TREATMENT OPTIONS AND DECISIONS; CRANIAL NERVES; SURGERY BENEFIT AND RISK ASSESSMENT.

gastritis INFLAMMATION of the lining of the STOMACH. There are two broad classifications of gastritis: erosive and nonerosive. The most common cause of erosive gastritis is repeated irritation from ingested substances such as ALCOHOL, aspirin, and NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS). The most common cause of nonerosive gastritis is INFECTION with *HELICOBACTER PYLORI*, the strain of BACTERIA that causes PEPTIC ULCER DISEASE. Occasionally viral infections can cause acute gastritis, which resolves when the infection runs its course. Autoimmune gastritis, in which the IMMUNE SYSTEM attacks the cells that form the mucosal lining of the stomach, interferes with the absorption of certain NUTRIENTS, notably vitamin B₁₂ (pernicious ANEMIA).

Symptoms include DYSPEPSIA (upset stomach), PAIN, NAUSEA, VOMITING, and a sensation of fullness. The diagnostic path may include BARIUM SWALLOW and endoscopic examination of the ESOPHAGUS, stomach, and DUODENUM (first segment of the SMALL INTESTINE and the site of peptic ulcer disease). The gastroenterologist may biopsy samples of stomach tissue. Treatment targets the underlying cause. Eliminating ingestion of the responsible substance often ends erosive gastritis. ANTIBIOTIC MEDICATIONS can eradicate *H. pylori*. Treatment for autoimmune gastritis focuses on countering any NUTRITIONAL DEFICIENCY that results as well as eliminating other sources of irritation to minimize gastric inflammation.

See also AUTOIMMUNE DISORDERS; COLITIS; **ENDOSCOPY**; GASTROENTERITIS; PANCREATITIS; STOMACH CANCER.

gastroenteritis INFLAMMATION of the SMALL INTESTINE. The most common cause of gastroenteritis is viral INFECTION, though sometimes BACTERIA OR PARASITES are responsible. The inflammation of the intestinal mucosa (mucus lining of the intestinal

wall) reduces the small intestine’s ability to absorb NUTRIENTS and fluid. People often refer to gastroenteritis as “stomach flu,” though this is inaccurate; the “flu” or influenza is a viral infection of the pulmonary system.

Symptoms and Diagnostic Path

Symptoms of gastroenteritis include DIARRHEA, abdominal cramping, and occasionally ABDOMINAL DISTENTION. Depending on the cause of the infection, the diarrhea can be profuse or bloody; bloody diarrhea requires medical evaluation. There may also be FEVER and VOMITING.

Symptoms that extend beyond two or three days in children or the elderly, or in a person of any age who cannot keep any fluids down, require medical evaluation to prevent DEHYDRATION.

The diagnostic path may include laboratory tests to determine the presence of pathogens (agents of infection) in the stool and blood tests to help identify the extent and nature of infection. The doctor may take stool samples or a rectal swab to determine whether bacterial or parasitic pathogens are present, which would require treatment with the appropriate medications. Bacterial gastroenteritis most often results from consuming contaminated food or water. The doctor may recommend ANTIEMETIC MEDICATIONS to quell nausea and ANTIDIARRHEAL MEDICATIONS to reduce diarrhea, depending on the cause and extent of the symptoms.

Noninfectious forms of gastroenteritis include Crohn’s disease and radiation gastroenteritis. Crohn’s disease is a component of INFLAMMATORY BOWEL DISEASE (IBD), which many doctors believe is an autoimmune disorder with a genetic component in which the IMMUNE SYSTEM attacks the intestinal mucosa. The attacks result in small ulcerations that often bleed. The enteric symptoms are chronic; treatment targets the underlying disease. Radiation gastroenteritis results from damage to the intestinal mucosa that occurs with RADIATION THERAPY to the abdomen, and may be acute (limited to the course of radiation therapy) or chronic (signaling permanent changes in the intestinal mucosa).

COMMON ENTERIC PATHOGENS

Pathogen	Type	Route of Infection
astrovirus	VIRUS	contaminated food or water person-to-person
calicivirus	virus	contaminated food or water person-to-person
<i>Cryptosporidium</i>	PARASITE	contaminated water animal-to-person person-to-person
<i>Cyclospora cayetanensis</i>	parasite	contaminated food or water person-to-person
enteric adenovirus	virus	contaminated food or water person-to-person
<i>Escherichia coli</i>	BACTERIA	contaminated food or water person-to-person
<i>Giardia lamblia</i>	parasite	contaminated water person-to-person
<i>Listeria</i>	bacteria	contaminated food person-to-person
<i>Microsporidia</i>	parasite	unknown
rotavirus	virus	contaminated food or water person-to-person
<i>Salmonella</i>	bacteria	contaminated food reptile-to-person
<i>Staphylococcus enterotoxin</i>	bacteria	contaminated food person-to-person

Treatment Options and Outlook

Adequate fluid replacement and other supportive measures are the only treatment necessary for viral gastroenteritis, which typically runs its course in three to five days. Young children, older adults, and people who have serious chronic health care conditions are at greatest risk for complications from viral gastroenteritis, though most people recover fully. Bacterial and parasitic gastroenteritis require treatment with the appropriate medications to eliminate the causative PATHOGEN,

and sometimes have a longer course of illness than viral gastroenteritis. Treatment for radiation gastroenteritis focuses on dietary management (eating frequent small meals and foods high in fiber) with ANTIDIARRHEAL MEDICATIONS to help control diarrhea.

Risk Factors and Preventive Measures

Viral gastroenteritis is highly contagious and often occurs in outbreaks, particularly in group settings such as schools, day cares, nursing homes, camps, and contained environments such as cruise ships. These methods can significantly reduce infectious gastroenteritis:

- proper food handling and preparation
- frequent and thorough HAND WASHING
- drinking WATER PURIFICATION (boiling, filtration, chemical)

See also AMEBIASIS; COLITIS; CYCLOSPORIASIS; FOOD-BORNE ILLNESSES; FOOD SAFETY; GASTRITIS; GIARDIASIS; LISTERIOSIS; PARASITE; SALMONELLOSIS; SHIGELLOSIS; WHIPPLE'S DISEASE.

gastroesophageal reflux disorder (GERD) A chronic condition in which gastric contents leak back from the STOMACH into the ESOPHAGUS. Because stomach juices are highly acidic, this backwash creates chemical BURNS in the delicate tissues of the esophagus. The lining of the esophagus lacks the protective mucus that safeguards the stomach from gastric acid, making it vulnerable to injury. Up to 40 percent of adults in the United States have GERD. Though GERD can develop in people of any age, including children, the likelihood of it doing so increases with age. Treatments to manage GERD include medical, surgical, and lifestyle methods.

Symptoms and Diagnostic Path

The symptoms of GERD often appear or are more severe following meals, when lying on the back, when bending over, and when lifting or straining. Many people experience more severe symptoms at night that awaken them from sleep. Typical GERD symptoms are chronic (ongoing) and include

- PAIN, pressure, or burning sensation in the mid-chest

- NAUSEA, and less commonly VOMITING, after eating
- regurgitation (reflux) of stomach contents up to several hours after eating that causes a bitter taste in the MOUTH and a burning sensation in the THROAT
- a sense of fullness in the stomach even when hungry

Some people also experience chronic sore throat or hoarseness resulting from the persistent reflux, or HICCUPS, likely due to irritation of the DIAPHRAGM, where the esophagus and stomach join, which is the site of the irritation. The diagnostic path may include BARIUM SWALLOW, gastroesophagoscopy (endoscopic examination of the esophagus and stomach), and breath or BLOOD tests for the presence of *HELICOBACTER PYLORI*. Because GERD is so common and the diagnostic procedures are invasive, doctors often use a trial of medication, such as H₂ ANTAGONIST (BLOCKER) MEDICATIONS or PROTON PUMP INHIBITOR MEDICATIONS (PPIs), to suppress gastric acid production and then assume a diagnosis of GERD if the medication relieves the symptoms.

Treatment and Outlook

Most people obtain full relief from their symptoms with a combination of medical treatments and lifestyle modifications. Many people find lifestyle modifications (diet, WEIGHT LOSS AND WEIGHT MANAGEMENT, SMOKING CESSATION) combined with ANTACIDS adequate, while other people require stronger medications such as H₂ blockers or PPIs. Many H₂ blockers are available in over-the-counter formulas. Reducing gastric acid significantly reduces the amount reflux that can backwash into the esophagus.

The most common surgical treatment for GERD that fails to improve with medication and lifestyle methods, fundoplication, reinforces the upper section of the stomach (the fundus) to increase tension on the lower esophageal sphincter. There are several fundoplication methods, some of which the surgeon can perform laparoscopically and others that require OPEN SURGERY. Another surgical option is endoscopic gastroplasty to repair or strengthen the lower esophageal sphincter. The

TREATMENTS FOR GERD

Medical Methods	Surgical Methods	Lifestyle Methods
H2 BLOCKERS	fundoplication	WEIGHT LOSS AND WEIGHT MANAGEMENT
PPIs	endoscopic gastroplasty	elevate head of bed
antibiotics for <i>H. PYLORI</i>		SMOKING CESSATION
ANTACIDS		avoid CAFFEINE and ALCOHOL
		reduce carbonated beverages
		stay upright for 2 hours after meals
		sleep lying on the left side
		avoid NSAIDs and aspirin

most common complications after surgery are INFECTION and difficulty swallowing.

Risk Factors and Preventive Measures

Doctors are uncertain what causes GERD to develop, though various factors appear to contribute. Among them are

- OBESITY
- cigarette smoking
- *H. pylori*
- ASTHMA
- eating within two hours of going to bed
- heavy ALCOHOL consumption

Preventive measures include avoiding or minimizing factors associated with GERD as well as eating smaller meals and getting regular physical exercise, which helps maintain effective PERISTALSIS and gastrointestinal motility (movement of food through the gastrointestinal tract).

See also [ACHALASIA](#); [BARRETT’S ESOPHAGUS](#); [ENDOSCOPY](#); [ESOPHAGITIS](#).

gastrointestinal bleeding Gross (obvious) or occult (microscopic) bleeding along any section of the gastrointestinal tract. Gross bleeding generally is obvious. Occult bleeding often occurs with intestinal polyps. FECAL OCCULT BLOOD TEST (FOBT) is one method used to detect microscopic BLOOD in the stool. Several kinds of FOBTs are available for home use, though it is imperative to follow up with the doctor when the results are questionable or positive.

Gastrointestinal bleeding can result from numerous conditions as well as excessive doses of anticoagulant medications or irritation from med-

ications such as aspirin and NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS). The most common sites are the STOMACH, DUODENUM, sigmoid COLON, and RECTUM. There are three ways in which gastrointestinal bleeding presents:

- hematemesis is the VOMITING of bright red blood, signaling bleeding from the upper gastrointestinal tract (usually the ESOPHAGUS, stomach or duodenum)
- hematochezia is the passing of bright red blood rectally, indicating bleeding from the lower gastrointestinal tract (usually the sigmoid colon or rectum) or from HEMORRHOIDS
- melena is the passing of dark, tarry stools that signal bleeding from the upper gastrointestinal tract

All gastrointestinal bleeding requires medical evaluation to determine its cause. Persistent bleeding, even when the amounts of blood appear small, results in ANEMIA. The diagnostic path may include ENDOSCOPY of the upper and lower gastrointestinal tracts, esophagogastroduodenoscopy (EGD) and COLONOSCOPY respectively, as well as BARIUM SWALLOW and BARIUM ENEMA. Treatment targets the underlying condition, and may include BLOOD TRANSFUSION when the blood loss is significant.

CONDITIONS THAT CAN CAUSE GASTROINTESTINAL BLEEDING

ANAL FISSURE	BARRETT’S ESOPHAGUS
COLITIS	DIVERTICULAR DISEASE
ESOPHAGEAL CANCER	GASTRITIS
HEMORRHOIDS	INFLAMMATORY BOWEL DISEASE (IBD)
INTESTINAL POLYP	PEPTIC ULCER DISEASE
STOMACH CANCER	

See also [ESOPHAGEAL VARICES](#); [HEMORRHAGE](#).

gastroparesis Slowed function of the [STOMACH](#) that delays the travel of gastric contents into the [DUODENUM](#). Gastroparesis results from disturbances of or damage to the [VAGUS NERVE](#) (the tenth cranial nerve), which carries the nerve impulses that accelerate [PERISTALSIS](#) (rhythmic contractions of the gastrointestinal tract). Gastroparesis most commonly occurs after a viral infection though also is a complication of [DIABETES](#), which damages nerve structures throughout the body. Other causes include sclerotic conditions such as [MULTIPLE SCLEROSIS](#) or [scleroderma](#), anticholinergic medications often prescribed to treat [PARKINSON'S DISEASE](#), inadvertent damage to the vagus nerve as a complication of thoracic or [HEART](#) surgery, and intentional interruption of the vagus nerve (vagotomy) to treat conditions such as [PEPTIC ULCER DISEASE](#). People who are on long-term [PARENTERAL NUTRITION](#) also often have gastroparesis.

The main symptom of gastroparesis is frequent [VOMITING](#) of undigested food hours after a meal.

Other symptoms may include lack of [APPETITE](#) due to sense of fullness, [NAUSEA](#), [ABDOMINAL DISTENTION](#), and unintended weight loss. Gastroparesis can quickly result in [DEHYDRATION](#), which can create significant disturbances of blood [GLUCOSE](#) and [INSULIN](#) levels in people who have diabetes. The first approach of treatment is to shift to eating numerous small meals throughout the day, attempting to slow the pace of ingestion to accommodate the stomach's slowed functioning.

Medications to stimulate gastrointestinal motility, such as metoclopramide ([Reglan](#)), may improve gastric emptying. Control of diabetes, which may require multiple insulin doses throughout the day, is crucial. If symptoms continue, the gastroenterologist may suggest a [jejunostomy tube](#), or feeding tube, that bypasses the stomach. Most people, however, achieve an acceptable resolution of their symptoms, even when gastroparesis persists, through nonsurgical approaches.

See also [CRANIAL NERVES](#); [ENTERAL NUTRITION](#); [NUTRITIONAL NEEDS](#); [PANCREATITIS](#); [RAPID GASTRIC EMPTYING](#).



heartburn See [DYSPEPSIA](#).

Helicobacter pylori The BACTERIA responsible for much PEPTIC ULCER DISEASE and STOMACH CANCER. Researchers isolated *H. pylori* in 1982, a discovery that dramatically altered the treatment approach to ulcers. Though researchers do not know how *H. pylori* enter the gastrointestinal system, they believe INFECTION occurs early in life in most people. The bacteria establish themselves in the lining of the STOMACH in the area called the pylorus, and often in the DUODENUM (first segment of the SMALL INTESTINE) as well. The presence of *H. pylori* causes irritation, which the body counters with an inflammatory response in an attempt to buffer the gastric mucosa from the irritation. Over time this pattern of irritation and INFLAMMATION results in ulcerative erosions of the mucosa, commonly called stomach ulcers.

The urea breath test is a simple, accurate, and fast way for doctors to determine whether *H. pylori* are present. The person drinks a solution or swallows a capsule containing urea tagged with a carbon isotope. *H. pylori* metabolize the urea, releasing carbon dioxide containing the carbon isotope. A machine analyzes breath samples to detect the presence of carbon isotopes in the carbon dioxide. Endoscopic biopsy, blood tests to detect *H. pylori* antibodies, and stool tests that detect *H. pylori* antigens are other methods to diagnose *H. pylori* infection. As well, these tests show whether treatment with ANTIBIOTIC MEDICATIONS has successfully eradicated the bacteria.

H. pylori are sensitive to several antibiotics though have the ability to rapidly adapt and develop resistance. For this reason doctors prescribe two kinds of antibiotic medications in com-

bination. Treatment also includes PROTON PUMP INHIBITOR (PPI) MEDICATIONS OR H2 ANTAGONIST (BLOCKER) MEDICATIONS to suppress gastric acid production, which makes the stomach a more hostile environment for the *H. pylori* and reduces irritation to the inflamed tissues or ulcers. *H. pylori* are also sensitive to the common ANTIDIARRHEAL MEDICATION bismuth subsalicylate (Pepto-Bismol). There are numerous treatment protocols for eradicating *H. pylori* that use these medications in various combinations. Once eradicated, *H. pylori* seem not to recur.

See also ANTIBODY; ANTIGEN; CANCER RISK FACTORS; [ENDOSCOPY](#); [GASTRITIS](#).

hemorrhoids Veins and related structures in and around the ANUS that distend and swell. Hemorrhoids can be internal or external. An old term for hemorrhoids that remains in common use is piles, a reference to the appearance of external hemorrhoids. Hemorrhoids alone do not cause symptoms; about two thirds of adults in the United States have hemorrhoids. Hemorrhoids cause PAIN, itching, and bleeding when they become inflamed, develop BLOOD clots, or prolapse (protrude). Factors that contribute to symptomatic hemorrhoids include

- chronic CONSTIPATION and straining with BOWEL MOVEMENTS
- sitting on the toilet for extended periods of time, which reduces blood circulation
- low fiber diet, which results in small, hard stools that can be difficult to pass
- PREGNANCY, which pressures the pelvic floor and can affect perineal blood flow
- INFLAMMATORY BOWEL DISEASE (IBD)

The doctor can diagnose hemorrhoids via physical examination of the anal area, including DIGITAL RECTAL EXAMINATION (DRE) or anoscopy, when symptoms are mild. Treatment attempts to shrink and soothe the irritated tissues. Topical preparations containing an anesthetic agent and hydrocortisone can provide prompt, short-term relief. A SITZ BATH, or simply soaking in the bathtub, relaxes the anal sphincter enough to calm the spasms that prolapsed or thrombosed (clotted) hemorrhoids cause. Dietary changes (such as increased fiber and fluids) combined with frequent physical activity (such as walking) help to reduce constipation, which relieves straining and pressure on the anorectal area. The doctor can ligate (band off), cauterize, freeze, or excise (cut out) hemorrhoids that fail to respond to conservative treatment approaches. In the vast majority of people, appropriate treatment and lifestyle modifications end symptoms.

See also [ANAL FISSURE](#); [ENDOSCOPY](#).

hepatic abscess A pocket of INFECTION that develops within the LIVER, also called liver ABSCESS. Though not common, hepatic abscesses can develop as a complication of GALLBLADDER DISEASE in which infection spreads through the BILE DUCTS to the liver. Symptoms include ABDOMINAL PAIN (often focused in the upper left quadrant), tenderness and rigidity, and FEVER. A person with a hepatic abscess often appears very ill. Abdominal ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, and MAGNETIC RESONANCE IMAGING (MRI) are among the diagnostic procedures that help detect hepatic abscess. Treatment is percutaneous aspiration (inserting a needle through the SKIN and into the abscess) or laparoscopic surgery to drain the collected pus, with intensive antibiotic therapy to eradicate the infection. An untreated hepatic abscess can quickly become life-threatening, as the liver's rich blood supply can carry the pathogenic bacteria throughout the body.

See also [ANTIBIOTIC MEDICATIONS](#); MINIMALLY INVASIVE SURGERY; SEPTICEMIA.

hepatic cyst A noncancerous growth, often fluid-filled, that develops in the LIVER. Most simple hepatic cysts cause no symptoms; they become apparent during diagnostic procedures, such as

abdominal ULTRASOUND, done for other reasons. When there are no symptoms, no treatment is necessary beyond regular monitoring (watchful waiting). A hydatid cyst contains the larvae of the PARASITE *Echinococcus granulosus*, acquired through contact with animal feces that contain the parasite's eggs, which migrate to the liver. A hydatid cyst grows slowly though can become large enough to hold a liter or more of fluid. Even when hydatid cysts show no symptoms, doctors remove them because they can cause life-threatening complications such as PERITONITIS or SEPTICEMIA if they rupture. Removal of a hepatic cyst is nearly always a laparoscopic surgery.

See also MINIMALLY INVASIVE SURGERY; [PERCUTANEOUS LIVER BIOPSY](#).

hepatitis INFLAMMATION of the LIVER. There are numerous kinds and causes of hepatitis. Most hepatitis results from specific viruses that cause infections of the liver, ALCOHOL abuse, and hepatotoxic drugs. Hepatitis is the leading cause of LIVER FAILURE, and reason for LIVER TRANSPLANTATION, in the United States.

Infectious (viral) hepatitis The viruses that cause viral hepatitis belong to several virus families: the picornavirus family, which causes hepatitis A; the hepacivirus family, which causes hepatitis B; and the flavivirus family, which causes hepatitis C.

Though these viruses are among the smallest researchers have yet detected, they cause a wide range of illnesses from COLDS to viral MENINGITIS to POLIO. Researchers refer to those that specifically target the liver as hepatotropic and label them alphabetically in the sequence of their discovery. Each individual VIRUS has unique characteristics that cause a particular pattern of disease. Researchers classify viral hepatitis according to the viral variant responsible for the disease response.

Five viruses identified as hepatotropic ("liver loving") cause 95 percent of the infectious hepatitis diagnosed in the United States: hepatitis A (HAV), hepatitis B (HBV), hepatitis C (HCV), hepatitis D (HDV), and hepatitis E (HEV). Hepatitis A and hepatitis E cause acute infection only and rarely cause permanent liver damage, though hepatitis A infection can cause serious illness and fatality. Hepatitis A accounts for more than 60

percent of hepatitis cases in the United States and hepatitis B for nearly 30 percent. Other identified hepatitis viruses (HFV and HGV) are rare in the United States. Hepatitis B and hepatitis C can be present without showing symptoms; about a third of people who have hepatitis B are carriers (the virus is present in their bodies and infects others, though does not cause illness in them). Though health agencies routinely test donated BLOOD, tissue, and organs for hepatitis (as well as numerous other infectious agents), people who receive donor substances face some risk of infection. Hepatitis C accounts for about 80 percent of such infections; new infections have become rare as a result of stringent donor substances screening. Hepatitis D can replicate only when hepatitis B is also present. It often causes “superinfection”—

acute disease with chronic hepatitis B infection. Hepatitis E occurs in outbreaks related to water contamination, such as might follow widespread flooding, and tend to be more common among people who contract the virus during travel to developing countries where COMMUNITY SANITATION is inadequate.

Viral hepatitis begins with an acute illness that lasts from 2 to 10 months, though in most people the acute phase resolves in 4 to 6 months. Chronic forms of hepatitis often follow infection with HBV and HCV, resulting in recurring episodes of symptoms. The repeated inflammation is very harmful to the liver, causing scarring (fibrosis) that eventually becomes CIRRHOSIS (SCAR tissue replaces liver tissue). The damage tends to be progressive, culminating in liver failure in about 25 percent of

Hepatitis Virus	Mode of Infection	Preventive Measures
hepatitis A (HAV)	fecal-oral food-borne person-to-person occupational exposure	vaccination frequent HAND WASHING and conscientious PERSONAL HYGIENE postexposure prophylaxis
hepatitis B (HBV)	blood sexual contact shared needles among illicit injected DRUG users perinatal (to infant at birth) hemodialysis occupational exposure	vaccination safer sex practices avoid sharing needles barrier precautions to prevent occupational exposure postexposure prophylaxis
hepatitis C (HCV)	blood sexual contact shared needles among illicit injected drug users perinatal (to infant at birth) hemodialysis occupational exposure	safer sex practices avoid sharing needles barrier precautions to prevent occupational exposure postexposure prophylaxis
hepatitis D (HDV)	blood shared needles among illicit injected drug users occupational exposure	HBV vaccination (HDV can infect people only already infected with HBV) avoid sharing needles barrier precautions to prevent occupational exposure postexposure prophylaxis
hepatitis E (HEV)	fecal-oral water	boiling water when contamination is possible

people who have chronic hepatitis. About 10 percent of people who develop chronic hepatitis subsequently develop LIVER CANCER. People who have chronic forms of hepatitis may show no signs or symptoms of disease though are carriers who pass the virus to others with whom they have close contact (particularly sexual contact).

Alcoholic hepatitis Alcohol is highly toxic to the liver. Chronic alcohol abuse results in repeated inflammation of liver tissue, with resulting scarring (fibrosis) that ultimately limits the liver's ability to function (cirrhosis). Liver damage that occurs is permanent and may lead to liver failure.

Hepatotoxic hepatitis The most common hepatotoxins resulting in hepatitis are acetaminophen (Tylenol) and NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) such as ibuprofen (Motrin). Other hepatotoxins include cleaning solutions, industrial pollutants, and carbon tetrachloride. Hepatotoxic hepatitis can result in rapid liver failure or lead to chronic hepatitis.

Symptoms and Diagnostic Path

The general symptoms of hepatitis are the same regardless of the cause and occur in four distinct stages:

1. Infective asymptomatic, in which the virus has invaded the liver and is replicating. During this stage the person is most highly infective.
2. Prodromal, in which infection has not yet manifested symptoms but the person begins to feel generalized malaise, loss of APPETITE, and aversions to certain foods (and often to cigarette smoke).
3. Active disease response, with characteristic symptoms that include JAUNDICE, dark urine, pale stools, FEVER, fatigue, and abdominal tenderness.
4. Recovery, during which the person continues to feel fatigue and malaise but liver functions are returning to normal, or liver failure, indicating the disease process has overwhelmed the liver.

Viral hepatitis remains infectious for as long as the virus is active in the body. With chronic forms of viral hepatitis, symptoms recur periodically. Alcoholic hepatitis and hepatotoxic hepatitis

remain in active disease state until the causative substance clears the body.

Treatment Options and Outlook

Treatment for hepatitis is largely supportive, consisting of fluid consumption, adequate nutrition, and rest. The course of acute disease may be mild and flulike or life-threatening, depending on numerous variables such as the cause and the individual's personal health status. People who have IMMUNE SYSTEM impairments, such as those who have HIV/AIDS, are very young, or are very old are at greatest risk for severe disease. ANTIVIRAL MEDICATIONS such as adefovir, ribavirin, interferon, amantadine, and lamivudine sometimes limit the course of active disease in chronic hepatitis (HBV and HDV). Liver damage due to hepatotoxic hepatitis may be so overwhelming as to require immediate liver transplantation.

Chronic hepatitis remains a significant lifelong threat to health. Those who have chronic infectious hepatitis can pass the disease to others. Regardless of cause, chronic hepatitis limits the liver's ability to function. Physiologic stress, such as alcohol consumption or taking certain medications, can seriously strain the liver's capacity. People who have chronic hepatitis may experience frequent bouts of fatigue. Many people are able to enjoy relatively normal lifestyles, though must remain mindful of situations and substances that could challenge the liver.

Risk Factors and Preventive Measures

The primary risk factor for infectious hepatitis is exposure to others who have hepatitis infections. For hepatitis A, this includes consuming foods handled in an unsafe manner by a person who already has hepatitis A infection or handling contaminated fecal waste (such as diapers). Those at risk for blood-borne hepatitis infections (HBV, HCV, HDV) include

- people who have unprotected sex with multiple partners (hepatitis B is especially common among men who have sex with men)
- people who inject illicit drugs and share needles, paraphernalia, and drugs
- people who undergo long-term hemodialysis to treat renal (kidney) failure

- infants born to infected mothers
- people who received organ transplants before 1992 or blood transfusions before 1987 (before stringent screening practices became available)
- people who work in health care and public safety

The most effective measures for protecting against infectious hepatitis are diligent PERSONAL HYGIENE (especially HAND WASHING) and vaccination. Vaccines are available to prevent infection with hepatitis A and hepatitis B. The hepatitis B VACCINE also protects against hepatitis D, which requires the hepatitis B virus to replicate. Hepatitis A and hepatitis E infection confer lifelong immunity. Measures to reduce the risk for noninfectious hepatitis center on eliminating or limiting exposure to hepatotoxic substances including alcohol. The herb MILK THISTLE (silymarin) helps to protect the liver from damage and to recover from damage that occurs. Many health experts recommend that people who have hepatitis or have exposure to hepatotoxins take milk thistle.

See also FOOD SAFETY; HEPATITIS PREVENTION; LIVER CANCER; LIVER DISEASE OF ALCOHOLISM; SHORT BOWEL SYNDROME.

hepatomegaly An enlarged LIVER. Hepatomegaly is a symptom of numerous conditions involving the liver. Its presence or absence has no correlation to the seriousness of the underlying liver disease. Because hepatomegaly is a symptom rather than a condition, it often resolves when the underlying condition comes under control. Chronic liver conditions may result in long-term hepatomegaly.

CONDITIONS THAT CAN RESULT IN HEPATOMEGALY

AMYLOIDOSIS	ANEMIA
CIRRHOSIS	congestive HEART FAILURE
HEMATOCHROMATOSIS	HEPATITIS
INFECTION	infectious mononucleosis
LEUKEMIA	LIVER CANCER
LIVER DISEASE OF ALCOHOLISM	LIVER FAILURE
REYE'S SYNDROME	SARCOIDOSIS
sclerosing cholangitis	STEATOHEPATITIS

See also: HEPATOTOXINS; JAUNDICE; MONONUCLEOSIS, INFECTIOUS; PORTAL HYPERTENSION; SPLENOMEGALY.

hepatotoxins Substances that damage the LIVER. A key role of the liver is to metabolize chemicals that it filters from the BLOOD. In the case of medications, this releases the therapeutic components into the bloodstream and channels the waste byproducts for appropriate elimination. Often the chemical interactions of these metabolic processes generate substances that poison the cells of the liver. Most drugs affect liver function to some degree; hundreds of them have short-term toxic effects and dozens cause permanent liver damage. The most common are ALCOHOL, acetaminophen, and NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS). Recreational drugs such as hallucinogenic mushrooms are especially hazardous to the liver. Industrial chemicals such as carbon tetrachloride and numerous environmental pollutants also cause the death of liver cells (hepatonecrosis).

Elevated levels of key liver enzymes in the blood provide early indication of hepatotoxicity. These include aspartate aminotransferase (AST), alanine aminotransferase (ALT), and glutamate oxaloacetate transaminase (GOT). Hepatotoxicity may also result in symptoms similar to those of HEPATITIS, such as JAUNDICE, NAUSEA, vomiting, and occasionally FEVER. Damage can be fairly immediate (within days to weeks of ingestion) or manifest months later. Regular alcohol consumption reduces the capacity of the liver to handle toxins, lowering the threshold at which damage occurs. Liver function often returns to normal when ingestion of the toxic substance ends and the liver completes all metabolic functions related to it, though hepatotoxic consequences can cause irreversible loss of liver function and even LIVER FAILURE. Many substances that damage the liver also damage the KIDNEYS. The herb MILK THISTLE, which contains silymarin, helps protect the liver from toxins.

See also ANALGESIC MEDICATIONS; CIRRHOSIS; HALLUCINOGENS; LIVER DISEASE OF ALCOHOLISM; OVERDOSE; POISON PREVENTION; RENAL FAILURE.

hereditary nonpolyposis colorectal cancer (HNPCC) A form of COLORECTAL CANCER predisposed by a mutation in the *mlh1* and *msh1* genes. These genes direct DNA repair mechanisms, the processes cells follow to correct mistakes that occur when they replicate their DNA codes during

cell reproduction, for cells in the mucous membrane lining of the COLON and RECTUM. Having the GENE mutations for HNPCC increases the likelihood that a person will develop colorectal CANCER before the age of 50 years. HNPCC accounts for about 5 percent of colorectal cancer in the United States as well as increased risk for GASTRIC CANCER, ENDOMETRIAL CANCER, and OVARIAN CANCER.

Cancer experts recommend annual COLONOSCOPY (examination of the colon with a flexible, lighted scope) to screen for colorectal cancer when HNPCC mutations are present, beginning at age 20 or upon identification of the mutations. Such screening permits the early detection and removal of the intestinal polyps that are the preliminary foundation for colorectal cancer. Polyps tend to progress to malignancy much faster in people who have genetic predisposition to colorectal cancer. Such aggressive screening has good potential for preventing colorectal cancer. GENETIC TESTING is important as well.

See also ADENOMA-TO-ADENOCARCINOMA TRANSITION; CANCER PREVENTION; CANCER RISK FACTORS; CELL STRUCTURE AND FUNCTION; FAMILIAL ADENOMATOUS POLYPOSIS (FAP); GENETIC DISORDERS; GENETIC TESTING; INHERITANCE PATTERNS; INTESTINAL POLYP.

hiatal hernia A weakening in the DIAPHRAGM, the muscular wall that separates the thoracic cavity (chest) from the abdominal cavity, that allows part of the upper STOMACH to slide upward into the chest. The weakening develops in the natural lapse in the diaphragm's continuity, called the hiatus, that allows the ESOPHAGUS to join the stomach. Hiatal hernia becomes more common with increasing age and often coexists with GASTROESOPHAGEAL REFLUX DISORDER (GERD). Most hiatal hernias do not present symptoms, though the GERD does. The hiatal hernia can worsen the symptoms of GERD by forming a pocket that traps the refluxed gastric contents, intensifying the duration of exposure the esophageal mucosa experiences. Risk factors for hiatal hernia include PREGNANCY (which pressures the diaphragm) and OBESITY.

BARIUM SWALLOW or esophagoscopy (endoscopic examination of the esophagus) can detect the presence of hiatal hernia. Unless there is risk for gastric or esophageal strangulation, in which a portion of the esophagus or stomach becomes

pinched off on the thoracic side of the diaphragm, lifestyle modifications such as weight loss and medications to treat associated GERD can successfully manage hiatal hernia. When there is a substantial risk for strangulation, such as with a large hernia, the gastroenterologist may recommend surgery to repair the hernia and prevent strangulation. Gastric or esophageal strangulation, though rare, requires emergency surgery.

See also ACHALASIA; BARRETT'S ESOPHAGUS; ENDOSCOPY; ESOPHAGITIS.

Hirschsprung's disease A CONGENITAL ANOMALY, also called congenital megacolon, in which the nerves that supply the lower COLON, typically the sigmoid colon and RECTUM, are missing. Nerves to the ANUS and anal sphincter are generally intact. The absence of nerves maintains the muscular wall of the lower colon in a state of perpetual contraction, bringing PERISTALSIS to a halt and causing digestive waste to accumulate. These events create pressure in the preceding segments of the colon, causing it to greatly dilate (megacolon). Untreated, this dilation results in TOXIC MEGACOLON, a massive dilation of the colon. Toxic megacolon is a life-threatening emergency that requires immediate surgery.

Symptoms include failure to pass MECONIUM (a newborn's first stool) within 48 hours of birth and ABDOMINAL DISTENTION. Hirschsprung's disease that involves only a short segment of the colon may remain undetected into childhood and even early adulthood, producing primarily symptoms of chronic CONSTIPATION and intermittent abdominal distress. The diagnostic path may include DIGITAL RECTAL EXAMINATION (DRE), abdominal X-rays, ULTRASOUND, or BARIUM ENEMA. Biopsy of the rectal wall confirms the absence of NERVE ganglia.

Treatment is surgery to remove the defective segments of bowel, connecting the ends of healthy bowel to maintain the integrity of the lower intestinal tract. The surgery restores normal bowel motility and function, allowing normal bowel movements. Sometimes the surgery takes place in two operations, the first to remove the defective bowel and the second to reconstruct the colon. A temporary COLOSTOMY allows digestive waste to leave the body during the interim HEALING phase. Most infants who undergo surgical repair before

toxic megacolon develops heal completely and without residual complications. Hirschsprung's disease often coexists with other congenital anomalies, notably DOWN SYNDROME.

See also GENE; INHERITANCE PATTERNS.

H2 antagonist (blocker) medications Medications that block molecular structures called histamine 2 receptors in the lining of the STOMACH. Histamines are chemicals called mediators that stimulate specific cells. Cells within the stomach's lining, called enterochromaffin-like (ECL) cells, release HISTAMINE in response to the digestive HORMONE gastrin. The histamine binds with H2 receptors on the parietal cells in the stomach. This binding stimulates the parietal cells to release hydrochloric acid into the stomach. H2 antagonists, or blockers, bind with the H2 receptors as well, blocking them from binding with endogenous histamine 2. The result is a decrease in acid production.

Other histamines are involved in different body functions. Histamine 1 (H1) stimulates smooth MUSCLE contraction and IMMUNE RESPONSE. H1 is familiar for its role in allergic response. Histamine 3 (H3) has NEUROTRANSMITTER activity. Histamine receptors are primarily unique; only H1 receptors accept histamine 1, only H2 receptors accept histamine 2, and only H3 receptors accept histamine 3. The ANTIHISTAMINE MEDICATIONS to relieve allergy symptoms have no effect on gastric acid produc-

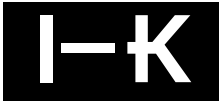
tion. Similarly, the H2 blockers have no effect on allergies.

Doctors may prescribe H2 blockers to treat GASTROESOPHAGEAL REFLUX DISORDER (GERD), PEPTIC ULCER DISEASE, chronic GASTRITIS, Crohn's disease that involves the stomach and ESOPHAGUS, HIATAL HERNIA, and other conditions in which excessive gastric acid causes symptoms or tissue damage. The four H2 blockers used in the United States are available in over-the-counter (OTC) and prescription strengths.

COMMON H2 BLOCKERS		
H2 Blocker	Prescription Strength	OTC Strength
cimetidine (Tagamet)	200mg, 300mg, 400mg, 800mg	100mg
famotidine (Pepcid)	20mg, 40mg	10mg
nizatidine (Axid)	150mg, 300mg	75mg
ranitidine (Zantac)	150mg, 300mg	75mg

H2 blockers, most notably cimetidine, interact with numerous other medications. ANTACIDS prevent the stomach from absorbing H2 blockers, significantly reducing the effectiveness of the H2 blocker. Side effects of H2 blockers may include dizziness, HEADACHE, and DIARRHEA. Changing to a different H2 blocker medication often resolves any side effects.

See also DIGESTIVE HORMONES; PROTON PUMP INHIBITOR (PPI) MEDICATIONS.



icterus See [JAUNDICE](#).

ileoanal reservoir An operation to connect the ILEUM, the final segment of the SMALL INTESTINE, directly with the anal canal (a short tract immediately before the ANUS) as an alternative to ILEOSTOMY when it is necessary to remove the entire COLON. The surgery may take place in one OPERATION or, more commonly, in two operations. First the surgeon removes the colon, leaving the anal canal, anus, and surrounding muscles intact. Then the surgeon uses the last 18 to 20 inches of the ileum to structure a pouch that replaces the RECTUM, and attaches it to the anal canal. The front end of the ileum remains as part of the small intestine. To allow these changes to heal the surgeon creates a temporary ileostomy, cutting the ileum and bringing the open end through an opening (stoma) in the abdominal wall. The ileostomy allows digestive waste, which, coming from the small intestine is fairly watery, to empty outside the body. When the ileoanal reservoir has healed, the surgeon performs a second operation to reconnect the ends of the ileum within the abdominal cavity and close the ileostomy.

With ileoanal reservoir the person retains control of the anal sphincter and has bowel movements, though stools are soft and bowel movements more frequent (7 to 10 per day). Bulking agents such as methylcellulose (Citrucel) or psyllium (Metamucil) help to solidify the stool. Foods that add bulk to the stool include bananas and rice. Risks of ileoanal reservoir include chronic INFECTION of the pouch, FECAL INCONTINENCE and stool leakage, and the need to make dietary changes (such as cutting out CAFFEINE and milk, which often cause diarrhea). Most people who

undergo ileoanal reservoir surgery return to a satisfactory QUALITY OF LIFE.

See also [COLOSTOMY](#); [FAMILIAL ADENOMATOUS POLYPOSIS](#); [INFLAMMATORY BOWEL DISEASE \(IBD\)](#).

ileostomy An OPERATION in which the surgeon brings the end of the ILEUM, the final segment of the SMALL INTESTINE, through the abdominal wall to exit outside the body. A pouch fastens with adhesive to the SKIN around the ileostomal opening, or stoma, to collect digestive waste. The waste is significantly more watery than stool.

An ileostomy is necessary after total bowel resection (removal of the COLON and RECTUM) such as to treat COLON CANCER, and may be temporary or permanent. An ileostomy is temporary when the surgeon can construct an ileoanal reservoir and permanent when this is not a viable option. A variation on an ileostomy that eliminates the need for ostomy bags is the continent ileostomy, in which the surgeon creates a collection pouch from a section of the ileum that remains inside the abdominal cavity. The surgeon sutures a valve in place that exits through the stoma. Periodically the person opens the valve to allow digestive waste to exit.

Many people find the adjustment to an ileostomy challenging. It represents a significant change to the body's appearance and function. The ileostomy, however, need not interfere with the regular activities of life including athletic pursuits, job and career, and sexual activity. An ostomy-care specialist, usually a registered nurse, will provide education about caring for the ileostomy.

See also [COLOSTOMY](#).

ileum The third, final, and longest segment of the SMALL INTESTINE. About 10 feet in length, the

ileum extends from the JEJUNUM to the CECUM. The ileum absorbs fats and fat-soluble vitamins as well as other remaining NUTRIENTS from the digestive content, which it then passes through the ileocecal valve into the cecum (the first segment of the COLON). Like the other segments of the small intestine, the ileum's walls contain extensive villi (fingerlike projections) that expand its surface area to increase its ability to absorb nutrients.

CONDITIONS THAT CAN AFFECT THE ILEUM

Crohn's disease	ILEUS
INTESTINAL ADHESIONS	LYMPHOMA
MALABSORPTION	SHORT BOWEL SYNDROME

For further discussion of the ileum and the small intestine within the context of gastrointestinal structure and function, please see the overview section "The Gastrointestinal System."

See also DUODENUM; ILEOANAL RESERVOIR; ILEOSTOMY; MINERALS AND HEALTH; VITAMINS AND HEALTH; NUTRITIONAL NEEDS.

ileus An obstruction or blockage of the intestinal tract. Ileus is potentially life-threatening and may require emergency surgery. Common causes include

- INTESINAL ADHESIONS
- tumors (benign or malignant)
- swallowed objects
- severe FECAL IMPACTION
- a BEZOAR that moves into the intestinal tract from the STOMACH

Symptoms include ABDOMINAL PAIN, VOMITING, DIARRHEA, and failure to have bowel movements. Typically BOWEL SOUNDS are absent in the intestinal tract beyond the obstruction, and the abdomen is rigid. The diagnostic path may include abdominal X-RAY, ULTRASOUND, or laparoscopic surgery. Treatment is nearly always surgery to remove the obstruction, often laparoscopic though sometimes OPEN SURGERY is necessary. Delays in surgery can result in tissue necrosis (death), requiring the surgeon to reconstruct a portion of the bowel and increasing the risk of INFECTION.

See also APPENDICITIS; BOWEL MOVEMENT; INTUSSUSCEPTION; MINIMALLY INVASIVE SURGERY; PERITONITIS.

indigestion See DYSPEPSIA.

inflammatory bowel disease (IBD) A chronic disorder in which INFLAMMATION develops along segments of the gastrointestinal tract. There are two forms of IBD, Crohn's disease and ulcerative colitis. Crohn's disease can affect any portion of the intestinal tract though most commonly involves the lower SMALL INTESTINE and upper COLON. Ulcerative colitis affects the colon including the RECTUM. Doctors and researchers believe IBD is an autoimmune disorder in which the IMMUNE SYSTEM may create antibodies that attack the intestinal mucosa (mucus lining of the intestinal walls). Researchers have detected several GENE mutations that correlate to Crohn's disease, and both Crohn's disease and ulcerative colitis have strong familial tendencies. Doctors consider the two conditions collectively because the disease processes, symptoms, and treatments overlap, though each condition has unique clinical features.

Symptoms and Diagnostic Path

Both forms of IBD generate ulcerative sores in the intestinal mucosa that cause irritation and inflammation. The resulting symptoms may include

- DIARRHEA, often bloody when IBD involves the colon
- rectal bleeding
- ABDOMINAL PAIN, sometimes intense
- unintended weight loss
- fatigue
- FEVER

The inflammation and bleeding typically result in ANEMIA, which is one reason for the fatigue. Other systemic changes related to the autoimmune disease process further contribute to fatigue. Alternating periods of symptoms and REMISSION characterize IBD. When IBD is in remission, gastrointestinal function is normal. When the disease is active, often referred to as an "attack," the severity of symptoms may range from manageable to debilitating.

The symptoms typical with IBD also are common with many gastrointestinal disorders. Determining the diagnosis requires a careful history of the pattern of symptoms, thorough physical examination, laboratory tests to look for markers of inflammation and autoimmune activity in the blood and in the stool, and imaging procedures to detect ulcerations and changes in the intestinal mucosa.

BARIUM SWALLOW with small bowel follow-through, in which the radiologist takes additional X-rays to follow the flow of barium as it leaves the **STOMACH** and passes through the small intestine, can visualize the ulcers and strictures (narrowed areas) that characterize Crohn's disease when it involves the small intestine. Sigmoidoscopy allows visual exploration of the lower colon, the site of ulcerative colitis. Esophagogastroduodenoscopy (EGD) may reveal involvement of the upper gastrointestinal tract in Crohn's disease.

These procedures help rule out other conditions as much as to confirm IBD. Doctors typically withhold these procedures during active flares of disease, however, to avoid further irritating the intestinal mucosa and because the inflamed mucosa presents an increased risk for inadvertent complications such as bowel perforation.

CLINICAL FEATURES OF IBD

Crohn's Disease	Ulcerative Colitis
"skip" pattern of intestinal involvement	continuous intestinal involvement
can affect any part of gastrointestinal tract	affects only the COLON, starts with the RECTUM
infiltrates multiple layers of mucosa	involves only the surface layer of mucosa
right lower abdominal mass	

Treatment Options and Outlook

Most people achieve relief from IBD symptoms through medications that suppress the immune response or target gastrointestinal function. Treatment protocols draw from various classifications of medications to address acute (active disease) and maintenance (remission) levels of care. Among them are **ANTIDIARRHEAL MEDICATIONS**, **anticholinergic medications**, **5-AMINOSALICYLATE (5-ASA) MEDICATIONS**, **CORTICOSTEROID MEDICATIONS**, **IMMUNOSUPPRESSIVE MEDICATIONS**, **ANTIBIOTIC MEDICATIONS**,

and **MONOCLONAL ANTIBODIES (MABS)**. While antibiotics treat enteric infections and abscesses that develop in the inflamed intestinal mucosa, they also seem to reduce complications and result in overall improvement of symptoms.

All of these medications have significant side effects. Because IBD is dynamic and unpredictable in its cycles of symptoms and remission, finding the most effective therapeutic balance remains a challenge. Medication regimens are highly individualized. As research progresses, new medications and treatment options enter the mix.

Surgery to remove the affected portion of the bowel becomes a treatment option to consider when damage to the intestine becomes extensive or symptoms no longer respond to medical treatments. For ulcerative colitis, surgery typically ends the disease process though the amount and location of bowel removed may have functional consequences, including colectomy (surgery to remove part or all of the colon). For Crohn's disease, surgery provides long-term relief though the disease may resurface or progress to involve remaining portions of the gastrointestinal tract.

Lifestyle is an important dimension of IBD not so much for its influence on the course of the disease but rather a result of IBD's influence on lifestyle. IBD is a long-term disorder for which, at present, there is no cure. The unpredictable nature of IBD's cycles and potential severity of attacks make it difficult for those who have it to stray far from its presence. Treatments attempt to manage symptoms for optimal **QUALITY OF LIFE** across the spectrum of the disease. During periods of remission most people who have IBD are able to participate fully in the activities they enjoy. During periods of active disease, many people find it difficult to maintain regular activities.

Complications associated with IBD are numerous, arising both from the disease and from its treatments. Autoimmune arthritis, notably **ANKYLOSING SPONDYLITIS**, often develops. Common with long-standing ulcerative colitis are the **EYE** infections **EPISCLERITIS** and **UVEITIS**, the biliary disorder **sclerosing cholangitis**, and significantly increased risk for **COLORECTAL CANCER**. Doctors recommend annual screening colonoscopy for people who have IBD with involvement of the colon or rectum beginning 8 to 10 years after diagnosis or earlier

COMMON IBD MEDICATIONS

Drug	Actions
5-aminosalicylates (5-ASAs) balsalazide (Colazal) Canasa suppository mesalamine (Asacol, Pentasa) olsalazine (Dipentum) Rowasa ENEMA sulfasalazine (Azulfidine)	local anti-inflammatory oral products coated to dissolve in the SMALL INTESTINE or COLON
anticholinergics atropine dicyclomine (Bentyl)	slow intestinal motility to reduce DIARRHEA systemic action
antidiarrheals loperamide (Imodium) diphenoxylate (Lomotil)	slow intestinal motility to reduce diarrhea gastrointestinal action
antibiotics metronidazole (Flagyl) ciprofloxacin (Cipro)	treat gastrointestinal INFECTION and abscesses
corticosteroids budesonide (Encort-EC) hydrocortisone (Hydrocort) hydrocortisone enema (Cortenema) prednisone prednisolone	systemic anti-inflammatory available for intravenous, oral, or rectal administration
immunosuppressives azathioprine (Imuran) methotrexate (Amethepterin) 6-mercaptopurine (Purinethol)	decrease immune activity
MONOCLONAL ANTIBODIES (MABS) infliximab (Remicade)	blocks action of TUMOR NECROSIS FACTOR (TNFS), which reduces INFLAMMATION

when other risk factors exist. People who have Crohn's disease are particularly susceptible to kidney stones (NEPHROLITHIASIS) and gallstones (cholelithiasis). Abdominal fistulas (abnormal openings between structures), anal fissures, and RECTAL PROLAPSE are also common complications with Crohn's disease. During disease flareups, some people who have IBD develop SKIN conditions.

Risk Factors and Preventive Measures

The most significant risk factor for IBD is family history, and researchers have identified several

genes that correspond to the Crohn's disease component of IBD. One in four who has IBD has a first-degree relative (parent, sibling, or child) who also has IBD. There are few other indications for why and how IBD develops, though most doctors believe a combination of factors convene to establish the disease process.

Neither the development nor outbreaks of IBD are preventable. Dietary precautions such as eating small meals and avoiding foods that irritate the gastrointestinal system (such as CAFFEINE, ALCOHOL, and

highly acidic foods) may help maintain overall gastrointestinal health. High-fiber foods often worsen the symptoms of ulcerative colitis and Crohn's disease that involves the colon. People who have IBD generally need **NUTRITIONAL SUPPLEMENTS**, particularly folic acid (folate) and iron, to offset nutritional deficiencies that result from **MALABSORPTION**. Smoking exacerbates Crohn's disease. In addition to irritating the gastrointestinal tract, alcohol interacts with many of the medications to treat IBD.

See also **ANTIBODY**; **APPENDICITIS**; **AUTOIMMUNE DISORDERS**; **CANCER PREVENTION**; **CANCER RISK FACTORS**; **CELIAC DISEASE**; **COLITIS**; **DIVERTICULAR DISEASE**; **ENDOSCOPY**; **GASTROENTERITIS**; **GASTROINTESTINAL BLEEDING**; **ILEUS**; **IRRITABLE BOWEL SYNDROME (IBS)**; **KAPOSI'S SARCOMA**; **NUTRITIONAL DEFICIENCY**; **NUTRITIONAL NEEDS**; **PERITONITIS**.

intestinal adhesions Areas of tissue that fuse together when **SCAR** tissue extends into normal tissue. Intestinal adhesions are most common in people who have had abdominal surgery (particularly multiple operations) though also may form with **ENDOMETRIOSIS**, **INFLAMMATORY BOWEL DISEASE (IBD)**, **CELIAC DISEASE**, and other circumstances in which there is damage to the abdominal tissues that generates scar tissue. Intestinal adhesions may cause abdominal discomfort during certain movements or activities or can become extensive enough to create partial or complete intestinal obstruction (**ILEUS**). Intestinal adhesions that interfere with digestive functions usually require surgery to clear away the scar tissue. Inherent in this treatment approach, however, is the risk for additional intestinal adhesions to form as a result of the scar tissue that develops during **HEALING**. Most intestinal adhesions do not cause functional problems. Surgeons typically remove any intestinal adhesions that are present whenever they perform other surgeries.

See also **SURGERY BENEFIT AND RISK ASSESSMENT**.

intestinal obstruction See **ILEUS**.

intestinal polyp A fleshy growth, also called an intestinal polypoid **ADENOMA**, that grows from the mucous membrane lining of the **COLON** or **RECTUM**. There are two common types of intestinal polyps, neoplastic adenomas and hyperplastic adenomas, both of which grow almost exclusively in the

colon. Neoplastic adenomas are neoplastic (abnormal growths that have no purpose or function in the body) and have the potential to turn malignant. Hyperplastic adenomas are not neoplastic and have no malignant potential.

Adenomas of either type arise from the epithelial cells, which make up the surfaces of membranes as well as the **SKIN**. Epithelial cells continuously renew themselves to replace worn and damaged epithelial tissues. Protein messengers tell healthy cells when to stop growing, containing the structures they form. When this regulatory mechanism goes awry cells continue to grow, forming abnormal structures such as adenomas. Adenomas, in the intestinal tract as well as elsewhere in the body, become more common with increasing age. Various circumstances converge that permit **ADENOMA-TO-ADENOCARCINOMA** transition. Though only a small percentage of intestinal polyps become cancerous, more than 95 percent of **COLORECTAL CANCER** evolves from intestinal polyps. Typically this transition takes 5 to 10 years or longer, during which biopsy can detect the changes in the cells (**DYSPLASIA**). Cancer experts recommend removal of all intestinal polyps to prevent this evolution. **COLONOSCOPY** is the most common method for detecting and removing intestinal polyps.

See also **ACTINIC KERATOSIS**; **AGING**, **GASTROINTESTINAL CHANGES THAT OCCUR WITH**; **CANCER PREVENTION**; **CANCER RISK FACTORS**; **FAMILIAL ADENOMATOUS POLYPOSIS (FAP)**.

intussusception A circumstance in which one portion of the intestine slides over another in telescopic fashion, creating an intestinal obstruction (**ILEUS**). Intussusception typically occurs in infants between the ages of 3 and 10 months, though can develop in children up to age six years. It is three times more common in boys than girls.

Intussusception is a life-threatening emergency that requires immediate treatment.

Symptoms include waves (paroxysms) of **PAIN** that at first appear to be colicky. Within 12 hours, however, the course shifts sharply from that of colic. **DIARRHEA** and **VOMITING** develop, and pain

becomes continuous. Stools often are watery and bloody, and may contain large quantities of mucus. Though intussusception is more common in children who have CYSTIC FIBROSIS or Meckel's diverticulum, or who experience blunt trauma to the abdomen, there are no certain predisposing factors.

BARIUM ENEMA provides the diagnosis, and, about 75 percent of the time, the treatment as well because the barium causes the bowel to expand back out. When the intussusception persists, the situation requires immediate surgery. Without treatment intussusception rapidly progresses to PERITONITIS and SEPTICEMIA, and usually is fatal. With appropriate treatment, nearly all infants experience full and uneventful recovery with no long-term consequences. Intussusception typically does not recur.

See also [DIVERTICULAR DISEASE](#).

irritable bowel syndrome (IBS) A constellation of symptoms that reflect functional disturbance of the gastrointestinal system. IBS is one of the most common gastrointestinal disorders that cause people to seek medical care, accounting for 10 percent of doctor visits each year. IBS symptoms are episodic and may range from mild to debilitating and typically manifest before age 35 years. IBS affects three times as many men as women.

Symptoms and Diagnostic Path

The hallmark symptoms of IBS are

- ABDOMINAL PAIN that goes away with bowel movements
- a change in the frequency and nature of bowel movements (DIARRHEA or CONSTIPATION that marks a change from usual bowel movements)
- mucus in the stool (mucorrhea)
- ABDOMINAL DISTENTION or sensation of bloating

Periods of exacerbation alternate with periods of REMISSION. In women, exacerbation may accompany other symptoms of PREMENSTRUAL SYNDROME (PMS). Stress, emotional or physical, is a significant catalyst of symptoms for many people who have IBS. The diagnostic path generally includes the gamut of gastrointestinal tests, though diagnosis of IBS relates to the length of time the person has had symptoms and the frequency with which

symptoms occur. Current diagnostic guidelines support a diagnosis of IBS when all of these four symptoms persist for longer than three months and doctors cannot detect any underlying pathologic reasons for the gastrointestinal disturbances.

Treatment Options and Outlook

Treatment targets symptoms and may include ANTIDIARRHEAL MEDICATIONS, ANTICHOLINERGIC MEDICATIONS to slow intestinal motility, and certain ANTI-DEPRESSANT MEDICATIONS that are successful in relieving symptoms in CHRONIC PAIN syndromes. Several medications specifically to treat IBS are available. There are significant risks and restrictions for some of these medications, and current regulatory and practice standards limit their use to people whose symptoms fail to respond to other treatments and interfere with daily living.

Alosetron (Lotronex) Alosetron specifically targets the neuroreceptors in the COLON to block the passage of NERVE signals that cause the colon to contract. This slows peristalsis only in the colon, increasing the amount of time digestive matter remains in the colon so the colon can absorb more water from it. Alosetron is available only for use in women who have debilitating diarrhea as the primary component of their IBS and under strict guidelines in which the prescribing doctor and the woman must agree to follow. Alosetron is not available for men because there is insufficient evidence of its effectiveness in men; clinical research studies enrolled primarily women. The most significant risks of alosetron are severe constipation that causes bowel obstruction (ILEUS) and ischemic COLITIS (blocked BLOOD flow to the colon that results in INFECTION).

Tegaserod (Zelnorm) Tegaserod mimics the action of serotonin, increasing the response of serotonin neuroreceptors in the intestinal tract. Serotonin is a NEUROTRANSMITTER most commonly recognized for its role in carrying nerve impulses related to emotion in the BRAIN. However, 95 percent of the serotonin in the body is concentrated in the gastrointestinal tract where it facilitates intestinal motility (peristalsis), gastric acid and other gastrointestinal fluid secretions, and the sensitivity of cells in the gastrointestinal tract to register pain. Like alosetron, tegaserod is available only for use in women who have debilitating diarrhea

and presents the risk of ischemic colitis. Tegaserod also can cause severe diarrhea.

Antidepressants Antidepressant medications affect the actions of several neurotransmitters, such as dopamine and serotonin, that play roles both in brain activity related to emotion and in gastrointestinal functions. The tricyclic antidepressants, such as amitriptyline (Elavil) and imipramine (Tofranil), have been instrumental in treating chronic pain syndromes and provide relief from IBS symptoms for some people. Selective serotonin reuptake inhibitor (SSRI) antidepressants, such as paroxetine (Paxil) and fluoxetine (Prozac), seem to have similar effects. These medications also treat the mild to moderate DEPRESSION that commonly accompanies IBS.

Lifestyle There is a strong correlation between episodes of IBS symptoms and stress. Stress management techniques, MEDITATION, guided imagery, BIOFEEDBACK, YOGA, ACUPUNCTURE, and therapeutic counseling are among the methods that can help keep symptoms in remission. Many people can control IBS largely through diet and lifestyle, after they understand the nature of the disorder and learn to recognize the triggers that bring on attacks of symptoms. Helpful dietary and lifestyle changes include

- reduce or eliminate CAFFEINE, which can contribute to diarrhea
- add fiber by eating more fruits, vegetables, and whole grain products, or by taking a fiber supplement such as psyllium (Metamucil) or methylcellulose (Citrucel)
- eliminate foods and beverages that cause intestinal upset (especially foods high in fat)
- maintain healthy weight
- develop a daily process for stress relief that may incorporate exercise, meditation, warm baths, designated quiet time or alone time, or other methods for de-stressing
- note circumstances and situations that appear to precipitate exacerbations of symptoms and work out approaches to mitigate them
- get 30 to 45 minutes of physical exercise, such as walking, daily to improve circulation, MUSCLE tone, and gastrointestinal function as well as to aid in relieving stress

Risk Factors and Prevention Efforts

Unlike many other chronic disorders affecting the gastrointestinal tract, IBS does not cause any damage to gastrointestinal tissue or increase the risk for CANCER. Even during attacks of symptoms, the bowel shows no evidence of INFLAMMATION or disease process. Tests that measure muscle contraction activity, usually performed only in clinical research studies because they have little diagnostic or therapeutic value, show accelerated peristalsis (intestinal motility).

A significant contingent of researchers and doctors believes IBS has a strong psychological component. This derives in part from the difficulty in identifying any organic, or physical, changes in the gastrointestinal tract that account for the symptoms and in part from a high correlation of diagnosed psychological conditions, such as GENERALIZED ANXIETY DISORDER (GAD) and depression, among people who have IBS. As well, a high percentage of people who have IBS have experienced physical or sexual abuse. Though few argue that these correlations exist, disagreement remains as to what the correlations mean in the context of either the psychological disorder or the IBS, especially in regard to treatment options.

One intriguing direction of research is the exploration of neurohormonal processes that handle both psychological and autonomic (involuntary) functions, raising the possibility of crossover between the two. Some clinical research studies have noted similarities in altered brain activity patterns, as detected via imaging procedures such as POSITRON EMISSION TOMOGRAPHY (PET) SCAN in people who have, independently, clinical depression and IBS. Other directions in research focus on gaining improved understanding of intestinal motility mechanisms. Though for some people IBS is a lifelong condition that requires vigilant management, for many others symptoms abate with an appropriate integration of medical and lifestyle interventions.

See also ACUTE STRESS DISORDER; BOWEL MOVEMENT; CELIAC DISEASE; DIET AND HEALTH; DIVERTICULAR DISEASE; FIBROMYALGIA; INFLAMMATORY BOWEL DISEASE (IBD).

jaundice Yellowish discoloration of the SKIN and whites of the eyes, also called icterus, resulting

from high levels of BILIRUBIN in the BLOOD. As well, the URINE may be dark brown or tea-colored and the stools pale, indicating a high concentration of BILE pigments dissolved in the urine and a lack of bile entering the intestinal tract. Intense itching (PRURITIS) often accompanies jaundice, the skin's reaction to the irritation of the bilirubin deposits. Bilirubin is a byproduct of the destruction of erythrocytes (red blood cells). The SPLEEN performs this destruction to rid the body of old erythrocytes that no longer function properly. The liver incorporates bilirubin into bile, which it then secretes into the gastrointestinal tract to aid in digestion as well as to excrete the excess as waste.

Jaundice indicates liver disease or GALLBLADDER DISEASE that interferes with this bilirubin handling, either in the breakdown stage (liver) or the elimination stage (GALLBLADDER). In most people the jaundice goes away with treatment of the underlying condition. Newborns commonly develop a form of jaundice not related to liver dysfunction called NEONATAL JAUNDICE or physiologic jaundice.

See also [CHOLESTASIS](#); [CIRRHOSIS](#); [HEPATITIS](#).

jejunum The middle segment of the SMALL INTESTINE, between the ILEUM and the DUODENUM. The jejunum is six to eight feet long and handles absorption of carbohydrates and proteins, as well as vitamins such as VITAMIN K and minerals such as iron. The jejunum's tissue composition and excellent blood supply allow it to be the source of tissue grafts for reconstruction of the pharynx and upper ESOPHAGUS after radical surgery to treat laryngeal CANCER (cancer of the THROAT). Health conditions that can involve the jejunum include INFLAMMATORY BOWEL DISEASE (IBD), CELIAC DISEASE, and MALABSORPTION disorders.

For further discussion of the jejunum and the small intestine within the context of gastrointestinal structure and function, please see the overview section "The Gastrointestinal System."

See also [BOWEL ATRESIA](#); [SHORT BOWEL SYNDROME](#).

kernicterus See [NEONATAL JAUNDICE](#).



laxatives Products to stimulate bowel movements. Laxatives work through various actions. Some help the stool to retain fluid, keeping the stool softer. Some lubricate the walls of the COLON, making it easier for digestive waste to move through the gastrointestinal tract. Others introduce fiber, which adds bulk to the stool as well as retains more fluid in the stool. Stimulant laxatives irritate the walls of the colon to accelerate PERISTALSIS (contractions of the bowel), which moves stool through the bowel. Laxatives intended to completely clear the colon, such as preparation for BARIUM ENEMA or COLONOSCOPY, are sometimes called cathartics or drastics because their actions are fast and intense. Laxatives come in oral

(tablets, powders, and liquids) and rectal (suppositories and enemas) preparations. They are available over the counter.

Doctors recommend attempting natural methods to encourage regular bowel movements before using laxatives. The gastrointestinal tract's rhythm correlates to the kinds and amounts of foods ingested, as well as to the frequency of meals. Though many people believe a daily bowel movement is "normal," normal is an individual measure that can range from two or three times daily to once every three days, depending on dietary habits. Using laxatives to structure daily bowel movements interferes with the bowel's natural rhythms. Over time, the bowel becomes "lazy"

COMMON LAXATIVES		
Kind of Laxative	Actions	Representative Products
stool softeners	add moisture to the stool	docusate sodium (Colace) docusate calcium (Surfak)
lubricants	lubricate the intestinal walls	glycerin suppositories mineral oil
bulking agents	add fiber to the stool, which increases bulk and draws moisture	bran calcium polycarbophil (FiberCon) methylcellulose (Citrucel) psyllium (Metamucil)
osmotic agents (hyperosmotics)	draw large amounts of fluid into the stool for rapid and thorough evacuation of intestinal contents	lactulose (Cephulac, Duphalac) magnesium citrate sodium citrate
STIMULANTS	irritate the walls of the colon to cause them to contract (PERISTALSIS)	bisacodyl (Dulcolax) casanthranol (Doxidan) senna (Senokot)

and does not contract unless a laxative stimulates it. Laxatives, and particularly suppositories and enemas, also can irritate the intestinal mucosa enough to cause chronic INFLAMMATION.

See also [BOWEL MOVEMENT](#); [DIARRHEA](#); [FIBER AND GASTROINTESTINAL HEALTH](#); [NUTRIENTS](#); [NUTRITIONAL NEEDS](#); [ROUTES OF ADMINISTRATION](#).

liver The largest internal organ in the body. Its soft, spongy tissue spreads like a flattened football between the DIAPHRAGM and the STOMACH, tucked protectively beneath the lower ribs on the right side of the abdomen. Weighing about three and a half pounds, the liver contains 15 percent of the body's blood (about a pint). About 60 percent of this blood is venous and comes from the gastrointestinal tract and SPLEEN, entering the liver via the portal VEIN. The venous blood delivers nutrients that the liver further metabolizes, the products of which it then sends back into the bloodstream. The hepatic ARTERY, which branches directly from the abdominal AORTA, delivers oxygenated blood to the liver to fuel the functions of its cells. On the underside of the liver is the GALLBLADDER, which concentrates and stores the BILE the liver produces.

The liver's two main lobes, the small left lobe and the large right lobe, support an intricate network of lobules, thousands of tiny communities of hepatocytes (the cells that carry out the liver's functions) that filter NUTRIENTS, wastes, BACTERIA, and toxins from the blood. The microscopic spaces between the lobules are the sinusoids, into which the blood from the portal vein drains. Each lobule is a hexagonal structure two layers of cells deep and several cells horizontally and vertically in a platelike configuration. At the vertical junctions of the lobules are the portal triads, each containing three microscopic structures: a venule, an arteriole, and a bile duct. The portal triads collect the substances the lobules produce and convey them to the larger vessels that will carry them out to the structures of the body. The membranous connective tissue that envelopes the liver also extends like a web through the liver, providing a supportive structure for the lobules, sinusoids, and portal triads.

The lobules are the work stations of the liver. They metabolize nutrients and toxins, and synthesize (manufacture) numerous substances includ-

ing amino acids, proteins essential for PLASMA production, lipoproteins, cholesterol, immune factors, CLOTTING FACTORS, LYMPH, and bile. The lobules convert GLUCOSE to glycogen, a storage form of glucose the body can draw from when blood levels of glucose fall, and glycogen back to glucose, processes that integrate closely with the balance of glucose and INSULIN in the blood. The lobules also deconstruct old erythrocytes (red blood cells) to recycle the iron and BILIRUBIN they contain. Specialized phagocytic ("cell eating") cells, called Kupffer cells, reside in the sinusoids to consume bacteria and cellular waste. The liver stores iron, glycogen, vitamin A and vitamin B₁₂, and other chemicals the body needs for cellular activities. The liver is unique among the body's organs in its ability to regenerate itself. This extraordinary capacity speaks to the significant extent of damage that must take place to permanently destroy liver tissue. Even so, the liver can meet the needs of the body as long as 25 percent of its cells remain functional.

COMMON CONDITIONS THAT CAN AFFECT THE LIVER

BILIARY ATRESIA	CHOLESTASIS
CIRRHOSIS	DIABETES
HEPATIC ABSCESS	HEPATIC CYST
HEPATITIS	LIVER CANCER
LIVER DISEASE OF ALCOHOLISM	PANCREATITIS
PORTAL HYPERTENSION	PRIMARY BILIARY CIRRHOSIS
PRIMARY SCLEROSING CHOLANGITIS	STEATOHEPATITIS

For further discussion of the liver within the context of gastrointestinal structure and function, please see the overview section "The Gastrointestinal System."

See also [BILE DUCTS](#); [ESOPHAGEAL VARICES](#); [HEPATOMEGALY](#); [HEPATOTOXINS](#); [JAUNDICE](#); [LIVER FAILURE](#); [LIVER FUNCTION TESTS](#); [LIVER TRANSPLANTATION](#); [NUTRITIONAL NEEDS](#); [VITAMINS AND HEALTH](#).

liver cancer Malignant growths in the LIVER. Liver CANCER may be primary (originates in the liver) or secondary (metastasizes, or spreads, from other locations in the body). Primary liver cancer is less common than metastatic liver cancer. Most primary liver cancer develops as a complication of chronic HEPATITIS B or hepatitis C INFECTION, conditions that repeatedly damage liver tissue, and

arises from the liver’s workhorse cells, the hepatocytes. Hepatocytes continually regenerate; researchers believe the continued replication of the hepatitis virus eventually creates changes in the processes of regeneration (cellular DNA alterations) that cause hepatocyte growth to become uncontrolled. Primary liver cancer is rare in people who have otherwise healthy livers. Because of its rich BLOOD supply and numerous functions related to blood filtration, the liver is a common site for metastatic cancers.

Symptoms and Diagnostic Path

Liver cancer typically does not present symptoms until the cancer is quite advanced, and even then symptoms often are vague. Such symptoms might include upper ABDOMINAL PAIN, ASCITES (fluid accumulation in the abdominal cavity), NAUSEA, lack of APPETITE, and JAUNDICE. The diagnostic path typically includes blood tests to assess liver function and hepatitis status, abdominal ULTRASOUND or COMPUTED TOMOGRAPHY (CT) SCAN, and PERCUTANEOUS LIVER BIOPSY.

Some doctors advocate regular testing to measure blood levels of ALPHA FETOPROTEIN (AFP), a protein that many liver tumors produce, in people who are at high risk for developing liver cancer (such as those who have chronic hepatitis or severe CIRRHOSIS). However, there is no consensus within the medical community as to the effectiveness of AFP screening for those not at high risk because numerous factors cause erroneous test results.

Treatment Options and Outlook

Treatment for liver cancer depends on whether the cancer is primary or secondary. Treatment for secondary liver cancer is generally palliative, aiming to relieve symptoms such as PAIN. For primary liver cancer, surgical removal of the tumor is the preferred option. However, people who have long-standing cirrhosis may have too much damage for the liver to remain functional after surgery. Large or multiple tumors also are difficult to remove without causing substantial damage to the remaining liver tissue. The surgeon may use RADIOFREQUENCY ABLATION or chemical ablation to kill tumor cells without removing the tumor; this is primarily a palliative treatment. LIVER TRANS-

PLANTATION is occasionally an option when the liver cancer is primary, small, and well contained.

Conventional external-beam RADIATION THERAPY often is not very successful in altering the course of liver cancer to increase survival, though it can shrink liver tumors to relieve pain and other symptoms. A precise technique for targeting liver tumors with radiation, three-dimensional conformal radiation therapy (3DCRT), shows promise for improving the therapeutic value of radiation therapy in liver cancer. Similarly, conventional CHEMOTHERAPY is not very effective against liver cancer, though in some people directly infusing chemotherapy agents into the hepatic ARTERY, called hepatic artery infusion (HAI) chemotherapy, has therapeutic benefit.

Because liver cancer tends to be either well advanced or metastatic at the time of its diagnosis, the overall outlook remains among the least positive despite the numerous advances in cancer treatments overall. The five-year survival rate, the standard measure for cancer treatment success, is about 30 percent when surgery can remove the tumor and about 5 percent when surgery is not a viable treatment option. Prevention efforts offer the greatest opportunity for defeating liver cancer.

RISK FACTORS FOR LIVER CANCER	
anabolic steroid use	chronic arsenic exposure
chronic hepatitis B infection	chronic HEPATITIS C INFECTION
CIRRHOSIS	HEMOCHROMATOSIS
LIVER DISEASE OF ALCOHOLISM	smoking and ALCOHOL abuse
vinyl chloride exposure	in combination
WILSON’S DISEASE	

Risk Factors and Preventive Measures

The most significant risk factor for liver cancer is infection with chronic hepatitis B or hepatitis C. Other circumstances that increase risk include cirrhosis, LIVER DISEASE OF ALCOHOLISM, exposure to hepatotoxic chemicals (especially arsenic, which remains a contaminant in water supplies throughout the United States as a result of past industrial waste practices, and the industrial chemical vinyl chloride), and smoking in combination with ALCOHOL abuse.

The single most important preventive measure for liver cancer is hepatitis vaccination to prevent

hepatitis B infection and appropriate measures to limit exposure to hepatitis C. People who already have chronic hepatitis, cirrhosis, or other conditions that increase the risk for liver cancer, the herb MILK THISTLE (silymarin) may help protect the liver from further damage. Other preventive measures include avoiding circumstances associated with liver cancer, notably excessive alcohol consumption. Though the number of people who develop primary liver cancer is rising, it remains less common than metastatic (secondary) liver cancer.

See also CANCER PREVENTION; CANCER TREATMENT OPTIONS AND DECISIONS; CELL STRUCTURE AND FUNCTION; ENVIRONMENTAL HAZARD EXPOSURE; HEAVY-METAL POISONING; HEPATITIS PREVENTION; METASTASIS; OCCUPATIONAL HEALTH AND SAFETY; SURGERY BENEFIT AND RISK ASSESSMENT.

liver disease of alcoholism Permanent damage to the LIVER that results from long-term, excessive ALCOHOL consumption. Alcohol is one of the most toxic substances ingested into the body. It enters the bloodstream unchanged, about 20 percent absorbed from the STOMACH and 80 percent from the SMALL INTESTINE. The liver must filter alcohol from the blood, a process that certain enzymes in the liver regulate. The enzymes limit the amount of alcohol the liver can extract, allowing alcohol to accumulate in the bloodstream.

The first of these enzymes, alcohol dehydrogenase (ADH), converts the alcohol into acetaldehyde. Acetaldehyde gives the breath of a person who has been drinking alcohol its characteristic odor. It is also a toxin, available as an industrial chemical for numerous manufacturing uses such as a solvent, hardener, and preservative. The second of these enzymes, aldehyde dehydrogenase, facilitates acetaldehyde's break down into acetic acid (the same acid found in vinegar) and acetylcoenzyme A. These substances are less toxic than acetaldehyde. Though aldehyde dehydrogenase works rapidly, it cannot convert all of the aldehyde before this toxic chemical causes the deaths of hepatocytes. Other enzymes in the liver further metabolize the acetic acid and acetate into GLUCOSE (energy) and carbon dioxide (waste).

With repeated exposure to acetaldehyde, structural changes take place in the liver. The first of these is the accumulation of fat in the liver. The

liver must direct nearly its full efforts to metabolize alcohol, in the effort to protect itself from the alcohol's toxic effects. As a consequence other metabolic functions in the liver slow, altering carbohydrate and lipid (fat) METABOLISM. The liver can metabolize alcohol at the rate of about 15 grams per hour, a pace that results in minimal hepatocytic damage. Alcohol consumption that exceeds this rate (equivalent to 1 ounce of 100-proof distilled spirits, one 12-ounce beer, or 4 ounces of wine) maintains alcohol circulation in the bloodstream until the liver can accommodate its metabolism. Repeated excessive alcohol consumption characteristically results in three liver disorders, which may exist singly or collectively.

Alcoholic hepatitis The HEPATITIS of ALCOHOLISM, also called Laennec's hepatitis, occurs when the repeated irritation of alcohol results in INFLAMMATION of the liver. When the flow of alcohol through the liver stops, symptoms abate and hepatocytes (the primary working cells of the liver) regenerate. Within a few months of alcohol cessation, the liver can restore itself to a normal level of function.

Alcoholic steatohepatitis Acetylcoenzyme A, one of the products of alcohol metabolism, interferes with the liver's synthesis and storage of fatty acids such that fatty tissue accumulates in the liver. Alcoholic STEATOHEPATITIS improves when the liver's metabolism of alcohol stops, and liver structure can return to normal with alcohol cessation.

Alcoholic cirrhosis Alcoholic CIRRHOSIS is a condition in which repeated INFLAMMATION (hepatitis) causes SCAR tissue to form and replace hepatocytes. As is the case with cirrhosis resulting from any cause, damage that has already occurred to the liver is not reversible. However, alcohol cessation halts the progression of cirrhosis to limit further damage.

Symptoms and Diagnostic Path

The symptoms of alcoholic liver disease are much the same as those of nonalcoholic liver disease and include JAUNDICE (yellowish discoloration of the SKIN), right upper ABDOMINAL PAIN, ASCITES (fluid accumulation in the abdominal cavity), NAUSEA, loss of APPETITE, and FATIGUE. The diagnostic path begins with LIVER FUNCTION TESTS and a thorough assessment of drinking habits. Additional diagnos-

tic procedures might include abdominal ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, OR PERCUTANEOUS LIVER BIOPSY.

Treatment Options and Outlook

Treatment is alcohol cessation and support for symptoms. The doctor may recommend an alcohol and SUBSTANCE ABUSE TREATMENT PROGRAM, counseling, 12-step program such as Alcoholics Anonymous, and other efforts to help maintain SOBRIETY. When liver disease of alcoholism reaches end-stage LIVER FAILURE, LIVER TRANSPLANTATION may be an option for a person who has maintained sobriety for at least six months and has a reasonable expectation of doing so following the liver transplantation. Though liver disease of alcoholism continues if alcohol consumption resumes, with alcohol abstinence the manifestations of liver disease are generally reversible (except cirrhosis).

Risk Factors and Preventive Measures

Chronic alcohol use is the only cause of liver disease of alcoholism. Though most often the use is excessive, alcohol-related damage can occur to the liver with moderate alcohol consumption that extends over a long period of time. Alcoholic steatohepatitis can develop in a person who consumes as few as four alcoholic drinks a week. The only, and absolute, preventive measure is abstinence from alcohol.

See also ENCEPHALOPATHY; HEPATOTOXINS.

liver failure The inability of the LIVER to function. Liver failure may be acute (comes on suddenly) or chronic (develops over time). Because the liver has the unique ability to regenerate, the damage it takes to cause liver failure is substantial. Liver failure generally occurs when more than 75 percent of the liver’s hepatocytes, the cells that carry out most of the liver’s functions, die, a circumstance called hepatocellular necrosis. LIVER TRANSPLANTATION is the only curative treatment for permanent liver failure.

The most common causes of hepatocellular necrosis leading to liver failure are

- ALCOHOL
- acetaminophen and especially acetaminophen OVERDOSE

- *Amanita* mushroom ingestion
- the illicit DRUG ecstasy (MDMA)
- isoniazid and rifampin in combination to treat TUBERCULOSIS
- industrial chemicals such as arsenic, phosphorus, carbon tetrachloride, and vinyl chloride
- disease processes

Hepatocellular necrosis is a SIDE EFFECT possible with numerous prescription medications, notably certain ANTIBIOTIC MEDICATIONS, “statin” lipid-lowering medications, and tricyclic ANTIDEPRESSANT MEDICATIONS. In some circumstances prompt medical intervention, such as with known overdose of drugs, can slow or halt hepatocellular necrosis and prevent liver failure, though liver damage may still occur. Such interventions might include aggressive medical efforts to remove or neutralize the responsible drug, administration of acetylcysteine for acetaminophen overdose, and liver hemodialysis (though this is of limited availability). In many circumstances, however, the destructive action of the toxin or the inflammatory process overwhelms the liver and attempted medical interventions have little effect.

CONDITIONS THAT CAN CAUSE LIVER FAILURE

BILIARY ATRESIA	chronic HEPATITIS
CIRRHOSIS	HEAT STROKE
HEMATOCHROMATOSIS	HEMORRHAGIC FEVER
LIVER CANCER	LIVER DISEASE OF ALCOHOLISM
PORTAL HYPERTENSION	PRIMARY BILIARY CIRRHOSIS
PRIMARY SCLEROSING CHOLANGITIS	REYE’S SYNDROME
secondary AMYLOIDOSIS	WILSON’S DISEASE

Acute liver failure Acute liver failure, also called fulminant HEPATITIS, develops in days to weeks. It nearly always follows a significant assault to the liver, such as drug overdose or severe trauma (such as gunshot wound) that destroys liver tissue. Hepatitis A INFECTION also can cause acute liver failure. Recovery without liver transplantation is uncommon and is most likely to occur with hepatitis A infection (about 50 percent recovery rate) and promptly treated acetaminophen toxicity.

Chronic liver failure Chronic liver failure, also called nonfulminant hepatitis, develops over

months. Repeated attacks of INFLAMMATION progressively kill hepatocytes until the level of hepatocytic function falls below 25 percent. In many situations a culminating event, such as a flare of hepatitis or an episode of acute alcohol INTOXICATION, pushes the liver across the boundary. CIRRHOSIS is the leading cause of chronic liver failure. Chronic liver failure without liver transplantation is fatal.

Symptoms and Diagnostic Path

People who are in liver failure are very ill. The most prominent symptoms are severe JAUNDICE (yellowish discoloration of the SKIN) and disturbances of cognitive and BRAIN functions, ranging from CONFUSION and HALLUCINATION to COMA, known collectively as hepatic ENCEPHALOPATHY. Neurologic signs that accompany these symptoms include disturbances of reflexes, tremors, and myotonus (MUSCLE spasms and rigidity). Evidence of clotting dysfunction, such as bruising and frank bleeding (internal or external), is also often present as the liver synthesizes many of the proteins and CLOTTING FACTORS necessary for COAGULATION. The diagnostic path includes LIVER FUNCTION TESTS that measure the levels of liver enzymes in the blood, toxicology screens to detect the presence of chemicals in the blood, and imaging procedures of the liver and the brain such as ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, and MAGNETIC RESONANCE IMAGING (MRI).

ALCOHOL AND ACETAMINOPHEN: A DANGEROUS COMBINATION

Regular ALCOHOL consumption, even as little as one drink a day, depletes the LIVER's supply of glutathione, an amino acid compound essential for metabolizing toxins. Insufficient glutathione exposes the liver to rapid hepatocellular necrosis, with resulting acute liver failure. People who drink regularly can experience acetaminophen OVERDOSE with as little as 4 grams of acetaminophen a day for three or four consecutive days, an amount that is well within the therapeutic dosage range.

Treatment Options and Outlook

Treatment options for liver failure are primarily supportive. Some people benefit from novel

approaches such as liver hemodialysis, which filters the blood similarly to renal dialysis (renal dialysis cannot remove the same substances from the blood), though such methods remain limited to major medical centers. Liver transplantation remains the only viable treatment for permanent liver failure, and the need for donor livers far outpaces the availability of donor organs. In some situations living donor liver segment transplantation, in which a living person donates a segment of his or her liver, is an alternative to cadaver donor liver transplantation.

Risk Factors and Preventive Measures

Chronic hepatitis infection and cirrhosis due to alcoholism are the leading risks for liver failure. Vaccination can prevent much, though not all, hepatitis. Drinking cessation can end the progression of cirrhosis, though damage already done is permanent.

See also ANALGESIC MEDICATIONS; COGNITIVE FUNCTION AND DYSFUNCTION; HEPATOTOXINS; ORGAN TRANSPLANTATION; REFLEX.

liver function tests A panel of BLOOD tests that measures the levels of ALBUMIN, BILIRUBIN, and certain LIVER enzymes in the blood. More specifically targeted tests further identify the reasons for abnormal results, as the findings may also indicate dysfunctions of other organs.

Reasons for Doing This Test

Liver function tests provide a general assessment of how effectively the liver is performing its metabolic tasks. They also allow the doctor to monitor the progression of liver disease and the effectiveness of treatment.

Albumin The liver synthesizes (produces) the key amino acids that make up albumin, the primary protein in blood PLASMA. Albumin transports numerous substances—including other proteins, NUTRIENTS, and hormones—through the blood. When albumin levels are low the blood cannot carry these substances, which has a variety of consequences throughout the body. Many liver conditions cause ASCITES (abdominal edema), in which a deficiency of albumin in the plasma allows plasma to seep across cell membranes to accumulate in the abdominal cavity. Decreased blood albumin

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levels suggest liver dysfunction. The normal range of serum albumin is 3.4 to 5.4 grams per deciliter (g/dL).

Bilirubin One key function of the liver is to complete the break down of old erythrocytes (red blood cells) to recycle their ingredients for other uses in the body. The **SPLEEN** initiates this process, splitting the **HEMOGLOBIN** erythrocytes contain into its core proteins, heme and globin, and extracting the pigment bilirubin from the heme. Bilirubin is a waste product that the liver chemically alters to use in synthesizing **BILE**. The chemically processed bilirubin is conjugated or direct bilirubin; bilirubin that circulates in the blood is unconjugated or indirect bilirubin.

A healthy liver excretes most of the conjugated bilirubin it produces in the bile. A damaged liver cannot keep up the pace of bile production, allowing conjugated bilirubin to escape into the blood.

Elevated circulation of conjugated, or direct, bilirubin suggests liver or **GALLBLADDER** dysfunction. The normal range of serum direct bilirubin is 0.0 to 0.4 milligrams per deciliter (mg/dL).

Enzymes Enzymes are catalytic substances that expedite chemical processes within the liver. In a healthy liver enzymes remain within the lobules, the working communities of hepatocytes. Hepatocytic damage results in enzymes leaking from the cells and spilling out into the blood. The commonly measured liver enzymes are

- the aminotransferases (also called transaminases), which catalyze amino acid **METABOLISM**—for example, aspartate aminotransferase (AST), also called serum glutamic oxaloacetic transaminase (SGOT), and alanine aminotransferase (ALT), also called serum glutamic pyruvic transaminase (SGPT)

LIVER FUNCTION BLOOD TESTS		
Blood Test	Normal Values	Liver Implications of Abnormal Findings
ALBUMIN	3.4 to 5.4 grams per deciliter (g/dL)	decreased level may suggest hepatocellular necrosis, HEPATITIS, CIRRHOSIS
alkaline phosphatase (ALP)	44 to 147 International Units per liter (IU/L)	elevated level may suggest hepatitis, cirrhosis, biliary obstruction, LIVER DISEASE OF ALCOHOLISM
alanine aminotransferase (ALT)/serum glutamic pyruvic transaminase (SGPT)	20 to 125 IU/L	elevated level may suggest hepatocellular necrosis, hepatitis, cirrhosis, HEPATOTOXINS
aspartate aminotransferase (AST)/serum glutamic oxaloacetic transaminase (SGOT)	10 to 34 IU/L	elevated level may suggest hepatocellular necrosis, hepatitis, cirrhosis, LIVER CANCER, liver disease of alcoholism
direct BILIRUBIN	0.0 to 0.4 g/dL	elevated level may suggest hepatitis, cirrhosis, biliary obstruction, gallstones, GALLBLADDER DISEASE, CHOLESTASIS
gamma-glutamyltranspeptidase (GGT)	0 to 51 IU/L	elevated level may suggest hepatitis, cirrhosis, liver cancer, cholestasis, hepatocellular necrosis, hepatotoxins
prothrombin time (PT)	11 to 13.5 seconds	delayed time may suggest hepatitis, cirrhosis, gallstones, biliary occlusion

- alkaline phosphatase (ALP), which also goes up in biliary obstruction (blockage of the flow of BILE)
- gamma-glutamyltranspeptidase (GGT)

Collectively elevated levels of these enzymes in the blood indicate damage to the liver that has caused the death of hepatocytes (hepatocellular necrosis). Individual elevations may indicate damage to other tissues in the body such as might occur in the HEART with HEART ATTACK. The AST to ALT ratio is also significant; a ratio greater than 2:1 is common with LIVER DISEASE OF ALCOHOLISM.

Prothrombin time The prothrombin time (PT) measures the amount of time it takes for the clotting process to take place in the plasma. The normal range (for a person who is not taking ANTICOAGULATION THERAPY) is 11 to 13.5 seconds. Clotting time longer than normal suggests a general dysfunction of the body's clotting mechanisms. Liver function becomes suspect with an elevated clotting time because the liver synthesizes many of the proteins (CLOTTING FACTORS) necessary for COAGULATION.

Preparation, Procedure, and Recovery

Liver function tests require a blood sample, typically drawn from a VEIN in the arm. No preparation is necessary and there is no recovery period.

Risks and Complications

Some people experience minor bruising at the site of the venipuncture, which usually heals in a few days (though liver disease that affects clotting mechanisms may extend HEALING).

liver hemodialysis A treatment for acute LIVER FAILURE that employs extracorporeal (out-of-the-body) filtration of the BLOOD to remove the toxins the liver otherwise would metabolize. LIVER hemodialysis is currently of limited availability and remains largely an investigational treatment. Two procedures are in use, the extracorporeal liver assist device (ELAD) and the bioartificial liver. Each uses a biological approach (cultured human cells or porcine cells) to emulate the functions of the liver's hepatocytes (the cells in the liver that filter the blood). These methods provide a "bridge" of limited filtration until liver transplantation becomes possible.

See also CARDIAC ENZYMES; VENTRICULAR ASSIST DEVICES (VADS).

liver transplantation An OPERATION to replace a diseased LIVER with a donor liver as a treatment for end-stage LIVER FAILURE. Following liver transplantation, most people are able to return to full and active lives though must continue taking medications to suppress rejection of the donor liver (IMMUNOSUPPRESSIVE THERAPY).

Surgeons performed the first successful liver transplantation in the United States in 1967. The risk of organ rejection curtailed transplantation as a permanent treatment for liver failure, however, until the advent of the immunosuppressive medication cyclosporine in 1979. Cyclosporine and its contemporary counterparts (such as tacrolimus, which debuted 10 years later) have made transplantation a viable, long-term solution. In 2004 doctors added the monoclonal antibody basiliximab to the immunosuppressive arsenal, reducing rejection to about 10 percent. Surgeons now perform more than 5,500 such operations each year, with liver transplantation as a therapeutic solution limited only by the availability of donor organs.

Donor livers are either cadaveric (harvested from donors after death) or living-donor segment (a living person donates part of his or her healthy liver). Living-donor segment transplantations are possible because the liver has the unique ability to regenerate. After a living donor segment transplantation, the donor's liver eventually restores itself to full size and function. Ideally, the segment implanted in the recipient does the same. This regenerative capability means, too, that livers transplanted into children will grow as the child grows.

There are two basic types of liver transplantation:

- orthotopic liver transplantation (OLT), in which the surgeon removes the diseased liver and replaces it with the donor liver
- heterotopic liver transplantation (HLT), in which the surgeon leaves the person's own diseased liver (the native liver) in place and attaches the donor liver (or liver segment) in a "piggyback" fashion

Donor organs must match BLOOD TYPE and, for OLT, body size. With HLT body size is less important because the surgeon can select a liver segment of the appropriate size. The surgery to transplant a liver takes between 4 and 12 hours in most circumstances. Recovery includes up to three weeks of hospitalization and several months for full recuperation. Most people are able to return to regular activities including exercise, work, sexual activity, and eating habits.

The risks of liver transplantation include bleeding, INFECTION, and rejection of the donor liver. Rejection may occur within days of the transplant or at any time after recovery, though IMMUNOSUPPRESSIVE MEDICATIONS reduce the likelihood. Symptoms of rejection include JAUNDICE, NAUSEA, FEVER,

and PAIN. These symptoms require immediate medical attention to salvage the transplant.

CONDITIONS FOR WHICH
LIVER TRANSPLANTATION IS AN OPTION

acute (fulminant) LIVER FAILURE	AMYLOIDOSIS
autoimmune HEPATITIS	BILIARY ATRESIA
chronic liver failure	CIRRHOSIS
glycogen storage disease	HEMOCHROMATOSIS
hepatitis B/hepatitis C	hepatotoxic liver failure
LIVER DISEASE OF ALCOHOLISM	noncancerous LIVER tumors
PRIMARY BILIARY SCLEROSIS	PRIMARY SCLEROSING
WILSON’S DISEASE	CHOLANGITIS

See also ORGAN TRANSPLANTATION; SURGERY BENEFIT AND RISK ASSESSMENT.

malabsorption Inadequate absorption of **NUTRIENTS** into the **BLOOD** circulation from the **SMALL INTESTINE** during digestion, also called malabsorption syndrome. Malabsorption may result from damage to the small intestine that restricts the surface area of the intestinal mucosa (lining) or may develop as a consequence of digestive enzyme deficiencies. **CELIAC DISEASE**, **LACTOSE INTOLERANCE**, **CYSTIC FIBROSIS**, **GASTROENTERITIS**, and **INFLAMMATORY BOWEL DISEASE (IBD)** are among the more common causes of malabsorption. Conditions affecting the **PANCREAS**, **LIVER**, and **GALLBLADDER** can result in secondary malabsorption. Untreated malabsorption characteristically causes **NUTRITIONAL DEFICIENCIES** and **MALNUTRITION**.

The diagnostic path may include stool analysis, blood tests, and **URINALYSIS**. The gastroenterologist may perform an **ENDOSCOPY** with biopsy when preliminary test findings are inconclusive. Treatment, which often includes a combination of dietary and medical management methods, targets any underlying condition. Secondary malabsorption generally goes away when the underlying condition improves. Severe malabsorption with malnutrition requires **PARENTERAL NUTRITION** (intravenous solutions) to replenish the body's nutrients. Malabsorption related to enzyme deficiencies often resolves with dietary changes alone.

See also **BORBORYGMUS**; **DIET AND HEALTH**; **DIGESTIVE ENZYMES**; **NUTRITIONAL NEEDS**; **PANCREATITIS**; **SHORT BOWEL SYNDROME**; **SMALL BOWEL TRANSPLANTATION**; **STEATORRHEA**; **WHIPPLE'S DISEASE**.

meconium The first stool a newborn passes, made up of **AMNIOTIC FLUID**, **BILE**, and mucus. Meconium resembles tar in consistency and color. Its passing is a key indicator of the infant's health and gastrointestinal patency (clear passage). Infants

with healthy gastrointestinal systems pass their first meconium stools within 24 hours of birth and may continue to pass meconium for two or three days. An infant that fails to pass meconium within 24 hours may have a congenital malformation of the gastrointestinal tract such as **BOWEL ATRESIA**. A complication common in infants who have **CYSTIC FIBROSIS**, a genetic disorder that affects multiple body systems, is **meconium ILEUS** in which impacted meconium obstructs the bowel. Enemas often relieve the impaction; when they do not, surgery is necessary.

See also **CHILDBIRTH**; **CONGENITAL ANOMALY**; **ENEMA**.

nasogastric aspiration and lavage The clinical term for the procedure commonly called "pumping the **STOMACH**." In nasogastric aspiration and lavage, the health-care provider inserts a narrow tube (catheter) through the **NOSE**, down the back of the **THROAT** and the **ESOPHAGUS**, and into the stomach. The stomach's contents are then sucked through the tube. The health-care provider may also use the tube to instill a rinsing solution, often a mixture of liquid and activated charcoal, into the stomach to absorb and neutralize remaining gastric content. Nasogastric aspiration and lavage is most commonly an emergency treatment for ingested toxins, including **DRUG OVERDOSE**, though also can help diagnose gastric bleeding.

See also **GASTROINTESTINAL BLEEDING**; **INGESTED TOXINS**.

nausea A sensation of queasiness and the feeling of being about to vomit. Though nausea feels as though it arises from the gastrointestinal tract, the signals that initiate its sensations originate in two areas of the **BRAIN**, the chemoreceptor trigger zone and the emetic (**VOMITING**) center. These areas are

bilateral, existing in pairs on each side of the brain. Both receive NERVE and chemical input from body systems. Nausea often precedes vomiting, the forceful expulsion of upper gastrointestinal contents. However, nausea also exists without resulting in vomiting. Many medications that suppress nausea and vomiting, called ANTIEMETIC MEDICATIONS, block the chemical and nerve signals entering or leaving the chemoreceptor trigger zone.

Nausea is typically a symptom, a reaction such as a medication SIDE EFFECT, or a response such as to an irritation of the gastrointestinal tract. Severe PAIN such as from migraine HEADACHE, HEART ATTACK, MENINGITIS, or injury (including postoperative pain) also activates the chemoreceptor trigger zone and the emetic center. The causes of nausea send different kinds of signals. Some antiemetic

medications, such as prochlorperazine (Compazine) and meclizine (Antivert), generally target a broad range of these signals. Other medications, such as those prescribed to treat CHEMOTHERAPY-induced nausea and vomiting (CINV) or radiation-induced nausea and vomiting (RINV), narrowly and specifically target certain chemoreceptors.

ACUPUNCTURE, an ancient Eastern method in which the practitioner inserts hairlike needles in designated locations, is highly effective for some kinds of nausea including CINV, RINV, motion sickness, and MORNING SICKNESS. Acupressure, which uses pressure applied over key acupuncture points, is also effective for many people. Other remedies for nausea include GINGER and “flat” cola drinks or cola syrup.

See also [CYCLIC VOMITING SYNDROME](#); FOOD-BORNE ILLNESSES; [GASTROENTERITIS](#).

pancreas An elongated gland with both endocrine and exocrine functions that lies beneath the STOMACH on the upper left side of the abdomen, beneath the lower ribs. Both realms of function play roles in digestion, though the endocrine functions of the pancreas are also significant for maintaining the body's GLUCOSE-INSULIN balance and for regulating cellular use of glucose.

The main body of the pancreas is a loose collection of secretory cells, looking somewhat like a mass of fish eggs, that produce DIGESTIVE ENZYMES and juices. These cells organize in lobular formations, called acini, around ducts that channel their secretions to the main pancreatic duct coursing through the center of the pancreas (hence their designation as exocrine). The pancreatic duct joins the common BILE duct from the GALLBLADDER just before the DUODENUM (the first segment of the SMALL INTESTINE), adding its juices to the bile that then flows into the duodenum.

Interspersed among the secretory cells are about a million clusters of specialized cells that produce the hormones INSULIN, GLUCAGON, and SOMATOSTATIN. Called the ISLETS OF LANGERHANS, these clusters are the endocrine glands of the pancreas. An extensive BLOOD supply infiltrates the islets, which secrete their hormones directly into the bloodstream (hence their designation as endocrine). These hormones regulate numerous functions of METABOLISM throughout the body, including many that take place in the gastrointestinal system.

Pancreatic Enzymes and Juices

The pancreas produces numerous enzymes essential for digestion. DIGESTIVE HORMONES trigger their release. Key among the digestive enzymes are

- proteases, notably trypsin and chymotrypsin, which break down proteins; to protect itself

from these proteases hydrolyzing its own tissue, the pancreas secretes them in proenzyme forms, trypsinogen and chymotrypsinogen, that an enzyme in the duodenum, enterokinase, activates

- pancreatic lipase, which breaks down dietary triglyceride into fatty acid molecules the intestinal mucosa can absorb
- amylase, which breaks down dietary starches (plant-based stored carbohydrates) into disaccharides (multiple molecule sugars) in preparation for further digestion later in the small intestine
- ribonuclease and deoxyribonuclease, which break down nucleic acids (chemicals that facilitate the body's use of proteins)
- elastase, which facilitates the break down of proteins into amino acids
- bicarbonate, which neutralizes gastric acid in the chyme (mixture of food and gastric juices) that flows from the stomach into the duodenum

Pancreatic Hormones

The primary hormones the pancreas produces are insulin, glucagon, and somatostatin. Insulin is key to carbohydrate and lipid (fatty acid) metabolism, in the gastrointestinal tract as well as at the cellular level throughout the body. The pancreas releases insulin in response to digestive hormones the gastrointestinal tract secretes as food enters the various stages of digestion. Insulin regulates glucose levels in the blood by controlling how much, and when, glucose enters the cells. It also signals the LIVER to convert excess glucose to the storage form glycogen. Somatostatin slows the release of insulin. Glandular tissue in the intestinal mucosa also produces somatostatin, which

acts to slow the release of other digestive enzymes as well. The pancreas releases glucagon when blood glucose levels fall. Glucagon signals the liver to convert glycogen to glucose.

COMMON CONDITIONS THAT CAN
AFFECT THE PANCREAS

DIABETES	gallstones in the common bile duct
PANCREATIC CANCER	pancreatic cyst
pancreatic pseudocyst	PANCREATITIS

For further discussion of the pancreas and the functions of the islets of Langerhans within the context of gastrointestinal structure and function, please see the overview section “The Gastrointestinal System.”

See also [DIABETES](#); DIET AND HEALTH.

pancreatic cancer Malignant growths of the PANCREAS. Pancreatic CANCER seldom shows symptoms until the cancer is well advanced or metastasized, making it among the most lethal cancers and the fourth leading cause of deaths from cancer in the United States. The one-year survival rate is about 24 percent.

When symptoms do appear as the cancer advances, they include

- JAUNDICE, a yellowish discoloration of the SKIN that results from the cancer compressing the common bile duct and blocking the flow of BILE into the DUODENUM
- ABDOMINAL PAIN that may radiate to the back
- digestive disturbances that result from the cancer’s interference with pancreatic enzyme production or blockage of the ducts that carry the secretions out of the pancreas

The diagnostic path includes imaging procedures such as ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, OR POSITRON EMISSION TOMOGRAPHY (PET) SCAN to determine the location and extent of the cancer as well as LYMPH NODE involvement and regional METASTASIS. Percutaneous (needle) biopsy confirms the diagnosis.

Treatment depends on how extensively the cancer has spread. Surgery is most effective when the cancer is small, remains confined to the pancreas, and is located in the head of the pancreas.

Pancreatectomy, partial or complete, is complex surgery with significant risks and consequences (including DIABETES). It is a viable option only when the surgeon is reasonably certain it will completely remove the cancer. About 90 percent of pancreatic cancers have metastasized by the time of diagnosis. CHEMOTHERAPY may be effective in achieving REMISSION. External beam RADIATION THERAPY can shrink the cancer to relieve symptoms.

There are few clear risk factors or screening procedures for pancreatic cancer. There is some evidence of a hereditary component to pancreatic cancer, as it appears to run in families, though researchers have yet to detect the responsible genes. In people at high risk for developing pancreatic cancer because of family history, some cancer experts suggest annual ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP). This endoscopic procedure allows the gastroenterologist to examine the pancreatic duct for signs of precancerous changes in the cells (DYSPLASIA). Areas of focus in research include GENE THERAPY and IMMUNOTHERAPY (also called biological therapy), though therapeutic application of these remains investigational.

See also CANCER TREATMENT OPTIONS AND DECISIONS; [ENDOSCOPY](#); LYMPH NODES; PANCREATITIS; RISK FACTORS FOR CANCER; STOMACH CANCER; SURGERY BENEFIT AND RISK ASSESSMENT.

pancreatitis INFLAMMATION of the PANCREAS that can be acute (comes on suddenly) or chronic (ongoing).

Acute pancreatitis can be life-threatening and requires emergency medical treatment.

Between them, excessive ALCOHOL consumption and gallstones account for more than 80 percent of pancreatitis. Other causes include CYSTIC FIBROSIS, viral INFECTION (notably with the MUMPS VIRUS), SIDE EFFECTS of certain medications, and trauma to the abdomen (particularly blunt trauma such as might occur in MOTOR VEHICLE ACCIDENTS). A good deal of the time doctors cannot identify the cause of pancreatitis.

Symptoms and Diagnostic Path

Acute pancreatitis makes a person very ill, with symptoms that include moderate to severe ABDOMINAL PAIN, ABDOMINAL DISTENTION; NAUSEA, VOMITING, and FEVER. Often the PULSE and respiration rate are rapid. When symptoms are severe, the person may be in SHOCK, which is a life-threatening emergency. The diagnostic path includes BLOOD tests to measure the levels of the DIGESTIVE ENZYMES amylase and lipase, which become significantly elevated with pancreatitis. ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) can often identify signs of inflammation and can help determine whether gallstones are obstructing the BILE DUCTS, a common cause of acute pancreatitis. ULTRASOUND OR COMPUTED TOMOGRAPHY (CT) SCAN also can provide therapeutically useful information.

People who have chronic pancreatitis may have intermittent upper ABDOMINAL PAIN, though with advanced damage to the pancreas pain is less common. The primary symptom of chronic pancreatitis is persistent weight loss despite adequate eating. This occurs because the damaged pancreas is unable to produce the digestive enzymes the SMALL INTESTINE needs to absorb nutrients, so consumed food passes through the gastrointestinal tract largely useless in the context of meeting the body's NUTRITIONAL NEEDS. The same procedures doctors use to diagnose acute pancreatitis help diagnose as well as monitor chronic pancreatitis. Specialized tests also can measure production of pancreatic enzymes.

Treatment Options and Outlook

Treatment for acute pancreatitis is primarily supportive, with intravenous fluids to restore fluid and electrolyte balance within the body as well as to deliver GLUCOSE. Surgery becomes necessary when there is bleeding in the pancreas. Though illness can be severe, most people recover without residual consequences. Some people do subsequently develop chronic pancreatitis. Other complications may include RENAL FAILURE and the development of fluid-filled pockets called pseudocysts that often become infected.

Treatment for chronic pancreatitis is elimination of any contributing factors (such as alcohol consumption or removal of gallstones), plus a high-carbohydrate, low-fat diet to get basic nutri-

ents into the body. Enzyme supplements can improve digestion. Complications include DIABETES (requiring INSULIN THERAPY) and progressive loss of pancreatic function.

Risk Factors and Preventive Measures

Excessive alcohol consumption and gallstones are the leading risk factors for pancreatitis; alcohol abstinence and appropriate treatment for gallstones eliminates them. Other causes of pancreatitis are less defined and thus more difficult to prevent. Prompt medical assessment of symptoms and appropriate treatment improve the likelihood for uneventful recovery.

See also ALCOHOLISM; ENDOSCOPY; PANCREATIC CANCER.

peptic ulcer disease A condition in which ulcers form in the lining (mucosa) of the lower STOMACH and upper DUODENUM (first segment of the SMALL INTESTINE). The two most common causes of peptic ulcer disease are INFECTION with *HELICOBACTER PYLORI* and chronic or long-term use of NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS). Peptic ulcer disease affects millions of Americans. In most situations, appropriate treatment cures the condition.

Symptoms and Diagnostic Path

The symptoms of peptic ulcer disease range from mild and intermittent to severe and unrelenting. Severe symptoms suggest a perforated ulcer, which carries the risks of bleeding and infection. A perforated ulcer requires immediate medical attention.

Typical symptoms of peptic ulcer disease include

- DYSPEPSIA (heartburn or stomach upset), commonly occurring one to three hours after eating or at night
- NAUSEA and VOMITING
- GASTROINTESTINAL BLEEDING
- loss of APPETITE or intolerance for spicy or fatty foods
- unintended weight loss

Symptoms typically improve with ANTACIDS or acid-reducing medications. Some people experience CHEST PAIN mistaken for HEART ATTACK.

ENDOSCOPY to examine the ESOPHAGUS, stomach, and duodenum often makes the diagnosis, allowing the gastroenterologist to visualize the ulcers and extent of damage. Biopsy of a tissue sample or an urea breath test can determine whether *H. pylori* infection is present.

Treatment Options and Outlook

H. pylori infection accounts for nearly 80 percent of peptic ulcer disease. Treatment with appropriate ANTIBIOTIC MEDICATIONS to eradicate the BACTERIA allows the ulcers to heal. Chronic NSAID use is the second-most common cause of peptic ulcer disease; ulcers typically heal when the person stops taking the NSAID. Regardless of cause, the treatment of choice for peptic ulcer disease is acid-reducing medication to decrease irritation to the damaged tissue.

Gastroenterologists typically prescribe H₂ ANTAGONIST (BLOCKER) MEDICATIONS OR PROTON PUMP INHIBITOR (PPI) MEDICATIONS for this purpose. After the ulcers heal, most people no longer need to take the medication. Severe ulcers may require surgery, particularly if they are bleeding. The primary complication of peptic ulcer disease is perforation (an ulcer that “eats through” or penetrates the wall of the duodenum or stomach), which can result in life-threatening bleeding and usually requires surgery. There also is some evidence linking long-term peptic ulcer disease, particularly that resulting from *H. pylori* infection, with an increased risk for STOMACH CANCER.

Risk Factors and Preventive Measures

Doctors once believed stress was the primary cause of peptic ulcer disease, though now know this is not the case. The causes of peptic ulcer disease, are largely treatable (*H. pylori* infection) or preventable (NSAID overuse).

See also GASTROESOPHAGEAL REFLUX DISORDER (GERD); MULTIPLE ENDOCRINE NEOPLASIA (MEN); RISK FACTORS FOR CANCER; ZOLLINGER-ELLISON SYNDROME.

percutaneous liver biopsy A diagnostic procedure for removing a tissue sample from the LIVER. The doctor typically performs percutaneous liver biopsy on an outpatient basis in a hospital setting. Most people prefer to receive a mild sedative before the procedure. After anesthetizing the

abdominal SKIN and tissue above the liver, the doctor makes a tiny incision and inserts a special biopsy needle. The needle withdraws a core of liver tissue, which a laboratory then analyzes to determine the nature and structure of cells and other substances it contains. Percutaneous liver biopsy helps diagnose numerous conditions affecting the liver, including HEPATITIS, CIRRHOSIS, LIVER FAILURE, STEATOHEPATITIS, and LIVER CANCER. Though minimally invasive, percutaneous liver biopsy exposes the liver to several risks including INFECTION, INFLAMMATION, and bleeding. These complications are uncommon though can be serious.

See also LIVER FUNCTION TESTS.

peristalsis The rhythmic waves of contraction that move food through the gastrointestinal tract. Pressure against the inner walls of the intestines, such as occurs when food enters an intestinal segment, signals the muscles to contract and relax in a progressive pattern. The muscles ahead of the pressure relax, widening the intestinal passage, and the muscles behind the pressure contract, narrowing the passage. This action “massages” the intestinal contents forward. Peristalsis is totally involuntary, under the control of the autonomic NERVOUS SYSTEM.

See also BORBORYGMUS; BOWEL SOUNDS.

peritonitis INFLAMMATION and INFECTION of the peritoneal membrane that encases the contents of the abdominal cavity. Peritonitis usually indicates a perforation of the intestinal tract that allows intestinal content, including normally present BACTERIA, to spill into the abdominal cavity. Such a breach may occur as the result of APPENDICITIS or COLITIS, or with INFLAMMATORY BOWEL DISEASE (IBD) OR DIVERTICULAR DISEASE that erodes through the wall of the intestine. Peritoneal ABSCESS also often causes peritonitis. Peritoneal dialysis for KIDNEY failure, which circulates fluid within the peritoneal cavity to draw toxins from the body, may introduce bacteria into the peritoneal cavity to cause peritonitis.

Peritonitis is potentially life-threatening and requires emergency treatment and usually surgery.

Symptoms often appear suddenly and are severe. Initially the perforation may provide relief because it releases pressure but the spreading infection quickly worsens symptoms. There is often abdominal rigidity and guarding (extreme resistance to having anyone touch the abdomen), ABDOMINAL DISTENTION, high FEVER, and signs of SEPTICEMIA (septic SHOCK) such as rapid PULSE and respiration. Blood tests and abdominal X-RAY or ULTRASOUND generally confirm the diagnosis. The infection paralyzes the intestine, halting PERISTALSIS and the absorption of fluids, nutrients, and electrolytes. Electrolytes are critically important for proper regulation of many body activities including those of the BRAIN and HEART. Treatment is immediate intravenous fluids to restore the body's electrolyte balance, ANTIBIOTIC MEDICATIONS to begin fighting the infection, and usually emergency surgery to drain the infection from the peritoneal cavity and remove any necrotic (dead) tissue or bowel. Recovery is not certain, and often complications remain following treatment, depending on the reason for the peritonitis.

See also PELVIC INFLAMMATORY DISEASE (PID); RENAL DIALYSIS.

portal hypertension High pressure in the portal VEIN, the large BLOOD vessel that carries blood from the abdominal organs to the LIVER. CIRRHOSIS, in which SCAR tissue replaces liver tissue as a consequence of repeated INFLAMMATION, is the primary cause of portal hypertension. Right HEART FAILURE also can cause portal hypertension.

About 40 percent of the blood that enters the liver does so through the portal vein. Blood drains into the portal vein from the digestive organs of the abdomen, carrying NUTRIENTS and metabolic wastes to the liver for processing. Though blood flows through the arteries under high pressure, the pressure within the veins is low and venous blood flow mostly relies on a combination of lower resistance, gravity, and valves within the veins to prevent backflow.

The spongy tissue of a healthy liver accepts blood flow from the portal vein in a smooth process, literally soaking in the blood and channeling it through the thousands of lobules that form the liver's interior architecture. The solid structure of scar tissue does not absorb blood like

the spongy tissue of the healthy liver, and blood must force its way around. The resistance that results causes the pressure within the portal vein to rise.

When scarring becomes severe, as in cirrhosis, the liver cannot contain the amount of blood attempting to enter and the blood backs up into the portal vein as well as the veins that feed into the portal vein. The walls of the portal vein stiffen against the resistance, which further raises pressure. Eventually the consequence of portal hypertension is twofold: blood cannot circulate through the liver and the supporting veins that feed into the portal vein distend and weaken. These VARICOSE VEINS typically protrude into the ESOPHAGUS (ESOPHAGEAL VARICES) and often bleed.

Symptoms and Diagnostic Path

The key symptoms suggesting portal hypertension are those of liver disease and may include

- JAUNDICE, a yellowish discoloration of the SKIN
- PRURITUS (widespread itching)
- fatigue and weakness
- ASCITES, an accumulation fluid in the abdomen
- evidence of GASTROINTESTINAL BLEEDING, which may appear as VOMITING blood (hematemesis) or passing dark stools (melena)

The doctor's examination can usually detect numerous signs of portal hypertension, such as abnormal PULSE, low systemic BLOOD PRESSURE (HYPOTENSION), and evidence of altered venous blood flow in the abdomen and lower extremities. The diagnostic path includes imaging procedures that can show the flow of blood through the liver, such as Doppler ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, OR MAGNETIC RESONANCE IMAGING (MRI). Endoscopic examination of the esophagus reveals esophageal varices, a conclusive sign of portal hypertension.

Treatment Options and Outlook

Bleeding esophageal varices require immediate medical attention. The gastroenterologist often can cauterize these during ENDOSCOPY. Vasodilator medications that relax the blood vessels, such as nitrates and beta blockers, relieve mild to moderate portal hypertension. Moderate to severe portal

hypertension requires surgical intervention. Shunts can help redirect the flow of blood into the liver and lower portal vein pressure. Sometimes removing the SPLEEN (SPLENECTOMY) and blood vessels surrounding the esophagus is necessary to control esophageal varices. The only curative treatment is LIVER TRANSPLANTATION, which, because donor organs are so limited, is a treatment of final resort when other therapies fail and LIVER FAILURE becomes life-threatening.

Medications and intermediary surgical procedures such as shunts can successfully manage portal hypertension in many people, allowing good QUALITY OF LIFE.

Risk Factors and Preventive Measures

Chronic liver disease and heart disease are the primary risk factors for portal hypertension. Lifestyle measures to minimize these conditions, and appropriate treatments to manage them when they do occur, significantly reduce the likelihood that portal hypertension will develop.

See also [CARDIOVASCULAR DISEASE PREVENTION](#); [HEMOCHROMATOSIS](#); [HEPATITIS PREVENTION](#); [LIFESTYLE AND HEALTH](#); [WILSON'S DISEASE](#).

primary biliary cirrhosis An autoimmune disorder in which chronic and progressive INFLAMMATION destroys the intrahepatic BILE DUCTS (bile ducts within the LIVER), blocking the flow of BILE. Primary biliary CIRRHOSIS appears to run in families, suggesting a hereditary component. Early symptoms include fatigue, tenderness or PAIN in the upper right abdomen, and itching (PRURITIS). Over time, signs of liver damage, such as JAUNDICE and HEPATOMEGALY (enlarged liver), emerge. Primary biliary cirrhosis is most common in women between the ages of 40 and 60.

The diagnostic path includes

- LIVER FUNCTION TESTS, which typically show elevations of the enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma-glutamyl transpeptidase (GGTP).
- BLOOD tests to measure the level of immunoglobulin (elevated) and detect the presence of antimitochondrial antibodies (positive)

- imaging procedures such as abdominal ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, or MAGNETIC RESONANCE IMAGING (MRI)
- PERCUTANEOUS LIVER BIOPSY

The progressive destruction of the bile ducts results in CHOLESTASIS and cirrhosis, leading ultimately to LIVER FAILURE. Complications include OSTEOPOROSIS (arising from the body's inability to metabolize vitamin D and calcium), PORTAL HYPERTENSION, ESOPHAGEAL VARICES, and primary LIVER CANCER.

There are currently few medical treatment options. The medication ursodiol (Actigall), sometimes taken to help dissolve gallstones, slows the progression of the inflammatory process in some people. ANTIHISTAMINE MEDICATIONS can help relieve the itching in the early stages; in later stages some people experience relief from itching with bile sequestrant medications such as cholestyramine and colestipol, which bind with bile in the gastrointestinal tract. The only curative treatment, however, is LIVER TRANSPLANTATION.

See also [AUTOIMMUNE DISORDERS](#); [BILIARY ATRESIA](#); [CANCER RISK FACTORS](#); [GALLBLADDER DISEASE](#); [PRIMARY SCLEROSING CHOLANGITIS](#).

primary sclerosing cholangitis A progressive and chronic condition in which segments of the BILE DUCTS become inflamed, causing SCAR tissue (sclerosis) that narrows and stiffens them. The scarring reduces and eventually destroys the ability of the ducts to carry BILE. About 75 percent of people who have primary sclerosing cholangitis also have INFLAMMATORY BOWEL DISEASE (IBD), suggesting a related autoimmune process. Primary sclerosing cholangitis is most common in men between the ages of 20 and 40.

In the early stages of the disease symptoms are mild and tend to wax and wane. Early symptoms may include fatigue, tenderness or PAIN in the upper right abdomen, and mild JAUNDICE (yellowish discoloration of the skin). Often the discovery of primary sclerosing cholangitis comes with elevated enzyme levels on LIVER FUNCTION TESTS done for other reasons, with confirmation by imaging procedures, such as ULTRASOUND or COMPUTED TOMOGRAPHY (CT) SCAN, and PERCUTANEOUS LIVER

BIOPSY. As more damage to the bile ducts occurs, symptoms intensify.

Medical interventions for primary sclerosing cholangitis are primarily supportive and aim to relieve symptoms such as PRURITIS (intense itching), which become more prominent as the condition progresses. The damage ultimately results in CIRRHOSIS and LIVER FAILURE. A significant risk during this progression is cholangiocarcinoma, a cancerous tumor that develops in the inflamed bile ducts. The course of the disease varies though tends to run about 10 years from onset of symptoms to liver failure. The only curative treatment is LIVER TRANSPLANTATION.

See also AUTOIMMUNE DISORDERS; BILIARY ATRESIA; CANCER RISK FACTORS; GALLBLADDER DISEASE; PRIMARY BILIARY CIRRHOSIS.

proctitis INFLAMMATION of the RECTUM that may also involve the ANUS. A number of circumstances may cause proctitis, including

- INFECTION, notably SEXUALLY TRANSMITTED DISEASES (STDs) such as CHLAMYDIA, GONORRHEA, and GENITAL HERPES
- inflammatory conditions such as INFLAMMATORY BOWEL DISEASE (IBD) and DIVERTICULAR DISEASE
- trauma to the anus and rectum
- bacterial INFECTION secondary to chronic inflammation or trauma
- RADIATION THERAPY (radiation proctitis)

Symptoms include the continuous sensation of needing to have a BOWEL MOVEMENT, CONSTIPATION, and rectal discomfort or PAIN. The doctor can usually diagnose proctitis via proctoscopy (viewing the anus and rectum endoscopically). Treatment targets the cause, which may include ANTIBIOTIC MEDICATIONS for infections and CORTICOSTEROID MEDICATIONS or other anti-inflammatory products for inflammation arising from trauma, radiation therapy, and inflammatory conditions of the gastrointestinal tract.

See also ANAL FISSURE; ENDOSCOPY; HEMORRHOIDS.

proton pump inhibitor (PPI) medications Medications that suppress gastric acid production in the STOMACH. Commonly prescribed PPIs available in the United States include

- esomeprazole (Nexium)
- lansoprazole (Prevacid)
- omeprazole (Prilosec)
- pantoprazole (Protonix)
- rabeprazole (Aciphex)

How These Medications Work

PPIs work by blocking the enzyme system that causes the parietal cells in the stomach's lining (gastric mucosa), called proton pumps, to produce and release hydrochloric acid. PPIs can block up to 99 percent of gastric acid production. PPIs also appear to slow the ability of *HELICOBACTER PYLORI* bacteria to move, reducing their ability to cause INFECTION. *H. pylori* infection is responsible for up to 80 percent of ulcers.

Therapeutic Applications

Doctors prescribe PPIs to treat PEPTIC ULCER DISEASE, GASTROESOPHAGEAL REFLUX DISORDER (GERD), and other conditions in which gastric acid becomes an irritation that causes symptoms such as INFLAMMATION and PAIN. PPIs are intended for relatively short-term use, during the HEALING phase of damaged gastrointestinal mucosa. After healing is complete, doctors recommend dietary modifications and H2 ANTAGONIST (BLOCKER) MEDICATIONS OR ANTACIDS for people who still need to suppress gastric acid.

Risks and Side Effects

PPIs have relatively few side effects or risks. Among the most common are HEADACHE, dizziness, fatigue, NAUSEA, ABDOMINAL PAIN, and DIARRHEA. No one PPI is more likely than another to cause side effects. Pregnant women should not take PPIs because researchers do not yet know whether these medications can harm the developing FETUS.

See also ESOPHAGITIS; GASTRITIS; GASTROENTERITIS.

R

rapid gastric emptying A disorder, also called dumping syndrome, in which food moves from the STOMACH into the SMALL INTESTINE incompletely digested, resulting in the small intestine attempting to digest solid food particles. Normally the digestive content that reaches the small intestine is fairly liquefied. The incomplete gastric digestion causes various gastrointestinal symptoms and leads to MALABSORPTION. Rapid gastric emptying typically occurs in people who have had stomach surgery, particularly BARIATRIC SURGERY for weight loss. Some research studies suggest that rapid gastric emptying in people who have not had stomach surgery may be an early sign of type 2 DIABETES. The diagnostic path may include gastroscopy and BARIUM SWALLOW to rule out other conditions. Treatment integrates dietary changes and medications to slow PERISTALSIS. Dietary changes include eating six small, low-carbohydrate meals throughout the day and drinking liquids between, rather than with, meals.

See also ENDOSCOPY.

rebound tenderness A clinical sign of PERITONITIS (generalized INFLAMMATION and INFECTION of the abdominal cavity). During abdominal palpation, the doctor presses slowly and firmly on the abdomen, then suddenly releases the pressure. The person feels a stabbing PAIN with release when the result is positive and notices no change when the result is negative. Rebound tenderness has a high level of accuracy for both positive and negative results. Rebound tenderness often appears as referred pain in appendicitis. The pressure and release action applied to the left side of the abdomen results in the person feeling pain on the right side of the abdomen, at the approximate location of the appendix.

See also [DIGITAL RECTAL EXAMINATION \(DRE\)](#).

rectal fistula An abnormal opening in the wall of the RECTUM, often connecting the rectum with another structure such as the URETHRA (rectourethral fistula), the VAGINA (rectovaginal fistula), or the ANUS (anorectal fistula). Rectal fistulas may be congenital or acquired. Congenital fistulas often occur in combination with other congenital anomalies, notably those affecting the HEART such as tetralogy of Fallot (a collective of malformations in the structure of the heart). Acquired rectal fistulas may be idiopathic (without detectable cause), though are more likely to occur in people who have inflammatory conditions that affect the gastrointestinal tract such as INFLAMMATORY BOWEL DISEASE (IBD). RADIATION THERAPY as treatment for PROSTATE CANCER, CERVICAL CANCER, OVARIAN CANCER, COLORECTAL CANCER, or other cancers in the abdomen can weaken the rectal wall, allowing fistulas to develop. As well, fistulas involving any portion of the gastrointestinal tract are frequent complications of HIV/AIDS.

Symptoms vary with the location of the fistula though often include FECAL INCONTINENCE or inappropriate presence of stool in the other involved structure. The diagnostic path may include DIGITAL RECTAL EXAMINATION (DRE), BARIUM ENEMA, and sigmoidoscopy (endoscopic examination of the lower COLON). Treatment is surgery to repair the fistula, which can sometimes be extensive when the fistula is long or deep. Potential complications vary according to the nature of the OPERATION necessary. In many people the surgical repairs end the symptoms and the person returns to his or her usual activities with no further problems. In some people, complications such as fecal incontinence arise or new fistulas occur.

See also [ANAL FISSURE](#); [CONGENITAL HEART DISEASE](#); [CYSTOCELE](#); [ENDOSCOPY](#); [HEMORRHOIDS](#); [ILEUS](#); [MECONIUM](#); [PROCTITIS](#); [RECTOCELE](#).

rectal prolapse Protrusion of the rectal mucosa (lining of the [RECTUM](#)) through the [ANUS](#). Rectal prolapse often affects women beyond [MENOPAUSE](#) who experienced trauma during vaginal [CHILDBIRTH](#) and have residual weakness of the pelvic structures. However, rectal prolapse occasionally affects men, usually those who are elderly. Long-term, chronic [CONSTIPATION](#) is a common factor when rectal prolapse occurs in women who have not given birth or in men. Prolapse of other pelvic organs, such as the [BLADDER](#) ([CYSTOCELE](#)), is also common. Rectal prolapse generally is apparent with physical examination, though the doctor often will perform sigmoidoscopy to rule out other conditions. Treatment is surgery to repair the rectal wall.

See also [ENDOSCOPY](#); [HEMORRHOIDS](#); [ILEUS](#); [RECTAL FISTULA](#); [RECTOCELE](#).

rectocele A weakness that develops in the wall of tissue that separates the [RECTUM](#) from the [VAGINA](#), called the rectovaginal wall, causing the rectum to protrude into the vagina. Rectocele, a type of [HERNIA](#), most commonly appears after [MENOPAUSE](#). Circumstances that chronically stress the muscles of the perirectal area, such as straining with bowel movements or frequent coughing due to pulmonary conditions, are frequent causes. Weakening of or damage to the perineal structures during vaginal [CHILDBIRTH](#) may also contribute to rectocele. Many women who have small rectoceles do not have symptoms. Larger rectoceles may produce symptoms that include the sensation of pressure in the vagina, pelvic [PAIN](#), painful vaginal intercourse, and occasionally [FECAL INCONTINENCE](#). Treatment options include [KEGEL EXERCISES](#) to strengthen the pelvic and vaginal muscles, weight loss to decrease stress on the pelvic muscles, and

the insertion of a [PESSARY](#), a fitted ring placed in the vagina to support the rectovaginal wall. Pessaries may cause irritation and [INFLAMMATION](#), however; and women may find them uncomfortable. Surgery to repair the herniation becomes an option when other treatments fail to correct the problem and symptoms continue.

See also [CYSTOCELE](#); [PELVIC EXAMINATION](#); [RECTAL PROLAPSE](#); [SURGERY BENEFIT AND RISK ASSESSMENT](#).

rectum The segment of the [COLON](#) between the sigmoid colon and the [ANUS](#). About six inches long, the rectum retains solid digestive waste until a [BOWEL MOVEMENT](#) expels it. The [SPINAL CORD](#) regulates the [NERVE](#) impulses that initiate the reflexive contractions of the rectum that result in bowel movements. The walls of the rectum are smooth and flexible, allowing it to expand to accommodate collected fecal material. The rectum is a frequent site of intestinal polyps and is vulnerable to [CANCER](#). Other health conditions that can involve the rectum include ulcerative [COLITIS](#), Crohn's disease, and [DIVERTICULAR DISEASE](#).

COMMON CONDITIONS THAT CAN AFFECT THE RECTUM

COLITIS	COLORECTAL CANCER
CONSTIPATION	DIARRHEA
DIVERTICULAR DISEASE	FAMILIAL ADENOMATOUS POLYPOSIS (FAP)
FECAL IMPACTION	HIRSCHSPRUNG'S DISEASE
INTESTINAL POLYP	PROCTITIS
RECTAL FISTULA	RECTAL PROLAPSE
RECTOCELE	SPINAL CORD INJURY

For further discussion of the rectum and colon within the context of gastrointestinal structure and function, please see the overview section "The Gastrointestinal System."

See also [BARIUM ENEMA](#); [CECUM](#); [COLONOSCOPY](#); [COLOSTOMY](#); [CYSTIC FIBROSIS](#); [DIGITAL RECTAL EXAMINATION \(DRE\)](#); [ENDOSCOPY](#); [ENEMA](#); [FECAL INCONTINENCE](#); [INTESTINAL POLYP](#); [SMALL INTESTINE](#).

S

short bowel syndrome Reduction in the structural or functional length of the SMALL INTESTINE that results in MALABSORPTION, chronic DIARRHEA, and other disturbances of digestion. MALNUTRITION is a common consequence. Short bowel syndrome most often results from surgery that removes segments of the small intestine as treatment for Crohn's disease, DIVERTICULAR DISEASE, cancers of the small intestine, traumatic injury, and other conditions that irreparably damage the small intestine. Short bowel syndrome was a common complication of a weight loss operation, jejunoileal bypass, that surgeons no longer perform. Functional short bowel syndrome also may develop following severe COLITIS (such as may occur with *ESCHERICHIA COLI* O157:H7 INFECTION) or radiation GASTROENTERITIS.

Treatment options for short bowel syndrome attempt to manage symptoms such as diarrhea as well as to meet NUTRITIONAL NEEDS. Most people who develop short bowel syndrome require PARENTERAL NUTRITION, a form of long-term intravenous feeding. Surgical options include operations to extend the remaining small intestine through various procedures and SMALL BOWEL TRANSPLANTATION or multivisceral transplantation (typically small bowel and LIVER or small bowel, liver, STOMACH, and PANCREAS). The extensive presence of lymphatic tissue in the gastrointestinal tract creates IMMUNE RESPONSE challenges with transplantation.

Liver and biliary dysfunctions (notably CHOLESTASIS) are common complications of short bowel syndrome, as the JEJUNUM and ILEUM produce a number of DIGESTIVE HORMONES that help to regulate liver activity and BILE release. When these segments of the small intestine are missing or no longer functional, the body has no secondary systems to synthesize these hormones. Long-term

total parenteral nutrition exacerbates liver and biliary dysfunctions. These factors tend to lead to LIVER FAILURE. Research directions for solutions to the challenges of short bowel syndrome therapies include explorations in IMMUNOTHERAPY (with a focus on suppressing the immune response in transplantation), pharmacotherapy (with a focus on supplemental hormones), and surgical methods that might improve small bowel function without transplantation.

See also CYSTIC FIBROSIS; GUT-ASSOCIATED LYMPHOID TISSUE (GALT); FOOD-BORNE ILLNESSES; INFLAMMATORY BOWEL DISEASE (IBD); MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT); RADIATION THERAPY.

sitz bath A small basin designed to accommodate the perineal and rectal areas, with the water level only to the hips. Numerous commercial products are available for ease of use at home. Placing a shallow amount of water in the regular bathtub accomplishes the same objective, which is to soothe irritated tissues caused by, for example, EPISIOTOMY incision, ANAL FISSURE, and HEMORRHOIDS. The water may contain medications or herbs for additional therapeutic effect.

See also MEDICINAL HERBS AND BOTANICALS.

small bowel transplantation Replacement of a diseased SMALL INTESTINE with a cadaver donor small intestine. Small bowel transplantation is a final treatment option for SHORT BOWEL SYNDROME or other circumstances in which there is total loss of small intestine structure or function. The gastroenterologist may consider small bowel transplantation when all other treatments, including total PARENTERAL NUTRITION, have failed. Small bowel transplantation is an extraordinarily complex procedure. The complication rate is high, and

at present the three-year success rate is about 50 percent.

The small intestine produces numerous DIGESTIVE ENZYMES and DIGESTIVE HORMONES necessary for proper function of the entire gastrointestinal tract. One challenge with small bowel transplantation is the restoration of this production. Another challenge is the abundance of lymphatic tissue in the intestinal mucosa (mucous membrane that lines the inside of the small intestine). Researchers do not yet fully understand the role of this tissue, called GUT-ASSOCIATED LYMPHOID TISSUE (GALT). However, GALT appears to intensify the IMMUNE RESPONSE typical with transplanted organs, requiring large doses of IMMUNOSUPPRESSIVE MEDICATIONS such as cyclosporine. These medications suppress immune activity throughout the body, not only in the intestinal tract, resulting in significant risk for INFECTION. Up to a third of people who receive small bowel transplantation experience complications including organ rejection and infection during the first year.

See also CYSTIC FIBROSIS; GASTROENTERITIS; ORGAN TRANSPLANTATION.

small intestine The segment of the gastrointestinal tract immediately following the STOMACH. The small intestine's three sections—DUODENUM, JEJUNUM, and ILEUM—perform about 85 percent of the digestive functions of the gastrointestinal tract. Food passes from the STOMACH to the duodenum, from the duodenum to the jejunum, and from the jejunum to the ileum. The small intestine loops and folds through the inner abdomen, with the COLON (large intestine) encircling it like a frame. Microscopic extensions, villi, arise from the mucosa, forming peaks and valleys that dramatically increase the surface area of the mucosa.

CONDITIONS THAT CAN AFFECT THE SMALL INTESTINE

BOWEL ATRESIA	CELIAC DISEASE
Crohn's disease	GASTROENTERITIS
ILEUS	LACTOSE INTOLERANCE
MALABSORPTION	PEPTIC ULCER DISEASE
WHIPPLE'S DISEASE	

A meal's transit time through the 18 or so feet of the small intestine is about 10 hours, during which intestinal mucosa (mucous membrane that lines

the intestinal tract) extracts all of the nutrients, many of the electrolytes, and much of the water.

For further discussion of the small intestine within the context of gastrointestinal structure and function, please see the overview section "The Gastrointestinal System."

See also ANUS; FOOD-BORNE ILLNESSES; INFLAMMATORY BOWEL DISEASE (IBD); IRRITABLE BOWEL SYNDROME (IBS); RECTUM.

steatohepatitis Fatty deposits throughout the LIVER, also called fatty liver, that create irritation and INFLAMMATION. Doctors believe steatohepatitis represents a malfunction of the body's lipid processing and transfer mechanisms, many of which take place in the liver. Steatohepatitis is common with long-term ALCOHOL use and ALCOHOLISM (alcoholic steatohepatitis). It also occurs without alcohol involvement (nonalcoholic steatohepatitis), notably with DIABETES (which alters lipid METABOLISM) and OBESITY.

The most common form of steatohepatitis, called macrovesicular because the fatty deposits are large, may not show symptoms. Rather, the doctor may detect it during physical examination as HEPATOMEGALY (enlarged LIVER). When symptoms are present they reflect noninfectious HEPATITIS: JAUNDICE (yellow discoloration of the SKIN), tenderness or PAIN in the upper right abdomen, fatigue, NAUSEA, and loss of APPETITE. LIVER FUNCTION TESTS may be inconclusive; ULTRASOUND or COMPUTED TOMOGRAPHY (CT) SCAN often reveals the fatty accumulations. PERCUTANEOUS LIVER BIOPSY confirms the diagnosis. The form of steatohepatitis associated with alcoholism, obesity, and diabetes is macrovesicular.

Steatohepatitis occasionally manifests as an acute illness with significant symptoms and rapid progression to clotting dysfunction (coagulopathy) and neurologic involvement (hepatic NEUROPATHY). This form of steatohepatitis, called microvesicular because the fatty deposits are small, can be fatal without appropriate supportive treatment until the liver recovers.

Macrovesicular steatohepatitis generally does not require treatment though treating any underlying condition helps restore normal lipid metabolism with the result that fatty acids move out of the liver. When alcohol consumption is a factor, steatohep-

atitis nearly always goes away with abstinence from alcohol though any CIRRHOSIS (replacement of liver tissue with SCAR tissue) that has already developed is permanent. Nonalcoholic steatohepatitis associated with diabetes generally improves with tighter management of the diabetes, and with obesity when weight loss occurs. Microvesicular steatohepatitis may require extensive support, including intravenous fluids and nutrients, during its acute phase. For many people recovery is complete and without residual damage to the liver.

See also DIET AND HEALTH; LIVER DISEASE OF ALCOHOLISM.

steatorrhea Excessive excretion of fat in the stool. Steatorrheic stools are often foamy and foul-smelling, and tend to break apart and float in the toilet bowl. Steatorrhea is a symptom of numerous gastrointestinal disorders including MALABSORPTION, CELIAC DISEASE, GALLBLADDER DISEASE, PANCREATITIS, and LIVER disease. Treating the causative condition ends the steatorrhea.

See also CONSTIPATION; CYSTIC FIBROSIS; DIARRHEA.

stomach The pouchlike organ that receives and digests food. The stomach can stretch up to six times its resting size to accommodate influxes of food and drink up to about the combined quantity of a gallon. Three layers of MUSCLE wrap around the deeply pitted gastric mucosa (mucous membrane lining of the stomach). The fibers of each muscle layer run in different directions: the layer innermost to the mucosa is oblique (diagonal), the middle layer of muscle is horizontal (encircles the stomach), and the outermost layer runs lengthwise. This arrangement allows the stomach to flex and contract in every direction to mix and break apart food particles.

CONDITIONS THAT CAN AFFECT THE STOMACH

BEZOAR	Crohn's disease
CYCLIC VOMITING SYNDROME	DYSPEPSIA
GASTRITIS	GASTROESOPHAGEAL REFLUX
GASTROPARESIS	DISORDER (GERD)
HIATAL HERNIA	PEPTIC ULCER DISEASE
STOMACH CANCER	ZOLLINGER-ELLISON SYNDROME

The stomach produces gastric acid, which is primarily hydrochloric acid, and several DIGESTIVE

ENZYMES. Though the stomach digests carbohydrates and some proteins, its primary role is to prepare food for the SMALL INTESTINE where the bulk of digestion takes place.

For further discussion of the stomach within the context of gastrointestinal structure and function, please see the overview section “The Gastrointestinal System.”

See also COLON; DIET AND HEALTH; DIGESTIVE HORMONES; ESOPHAGUS; GASTRECTOMY; *HELICOBACTER PYLORI*; H2 ANTAGONIST (BLOCKER) MEDICATIONS; INFLAMMATORY BOWEL DISEASE (IBD); NAUSEA; NUTRITIONAL DEFICIENCY; PROTON PUMP INHIBITOR (PPI) MEDICATION; VOMITING.

stomach cancer Malignant growths that occur in the STOMACH. Stomach CANCER is seventh among deaths from cancer in the United States. About 90 percent of stomach cancers are adenocarcinomas, malignant growths that originate in the glandular cells that carpet the gastric mucosa. These are the cells that produce the stomach's acid and mucus, as well as DIGESTIVE ENZYMES. Though stomach cancer readily metastasizes (spreads) to other tissues and organs, the stomach is seldom the site of secondary cancers that originate elsewhere in the body.

Though the causes of stomach cancer remain a mystery, researchers do know certain factors alter the DNA of cells in the stomach in ways that result in the uncontrolled growth that characterizes cancer. These factors cause chronic irritation to the stomach tissues. They include

- INFECTION with *HELICOBACTER PYLORI*, believed to cause about 85 percent of PEPTIC ULCER DISEASE
- a diet high in red meats, well-done barbecued meats, and smoked meats and fish that contain nitrates or nitrites (which convert to carcinogenic substances during the digestive action of gastric juices) as preservatives
- the combination of cigarette smoking and excessive ALCOHOL consumption
- untreated or poorly controlled GASTROESOPHAGEAL REFLUX DISORDER (GERD) or Crohn's disease

Symptoms and Diagnostic Path

Symptoms of early stomach cancer are often vague and nonspecific, such as DYSPEPSIA, NAUSEA

after eating, and a sense of fullness after eating only a small amount of food. Early stomach cancers often cause microscopic bleeding that a **FECAL OCCULT BLOOD TEST (FOBT)** can detect. As the cancer becomes more advanced, symptoms may include

- PAIN in the upper left abdomen
- VOMITING after meals
- dyspepsia that does not go away with antacids, eating, or medications to reduce acid in the stomach
- unintended weight loss
- blood in the vomit or in the stools, which may manifest as “coffee grounds” or tarry stools
- fatigue and weakness

The diagnostic path may include **BARIUM SWALLOW**, upper gastrointestinal **ENDOSCOPY** with biopsy, and **COMPUTED TOMOGRAPHY (CT) SCAN** OR **MAGNETIC RESONANCE IMAGING (MRI)**. The biopsy confirms the diagnosis and identifies the kind of cancer. The pathologic examination of the tissue sample also establishes the extent to which the cancer likely

has spread, called cancer staging. The cancer’s stage helps determine treatment options and protocols (standards of practice), and expectations about outlook (prognosis).

Treatment Options and Outlook

The main treatment for nearly all stages of stomach cancer is surgery to remove the cancerous tumor, involved tissues, and adjacent structures such as **LYMPH NODES** and fatty tissue. Surgery is curative for stomach cancer detected very early (stage 0). For stage 1, 2, and 3 stomach cancers oncologists recommend **CHEMOTHERAPY** and **RADIATION THERAPY** after surgery. The chemotherapy drugs commonly used to treat stomach cancer are 5FU, cisplatin, epirubicin, and etoposide, which the oncologist may administer individually (particularly 5FU for stage 1 cancers) or in combination with one another.

The surgical options for stomach cancer include

- endoscopic resection, in which the surgeon removes the tumor and a safe margin of stomach tissue endoscopically

BASIC STAGING OF STOMACH CANCER

Stage	Meaning	Treatment Protocol
stage 0	CANCER is in its earliest stages, completely confined to the gastric epithelium (lining of the STOMACH); also called CARCINOMA in situ	endoscopic resection, partial GASTRECTOMY , or total gastrectomy to remove the cancerous tumor
stage 1	cancer involves the gastric mucosa but remains confined to the stomach	partial or total gastrectomy with removal of adjacent fatty tissue and lymph nodes
stage 2	cancer extends into and beyond the MUSCLE layers of the stomach and may involve up to 15 adjacent LYMPH NODES	partial or total gastrectomy with extensive removal of adjacent fatty tissue and lymph nodes RADIATION THERAPY OR CHEMOTHERAPY ; occasionally a combination of both
stage 3	cancer extends beyond the stomach into adjacent lymph nodes and nearby organs such as the SPLEEN , LIVER , PANCREAS , or intestine	total gastrectomy with extensive removal of adjacent fatty tissue and lymph nodes surgery to remove tumors in other organs radiation therapy and chemotherapy
stage 4	cancer has spread from the stomach to other organs throughout the body	palliative surgery, chemotherapy, or radiation therapy to relieve symptoms, obstruction, and bleeding that may occur

- partial GASTRECTOMY, in which the surgeon removes the section of stomach containing the tumor
- total gastrectomy, in which the surgeon removes the entire stomach and an area of surrounding adipose (fatty) tissue called the omentum
- lymphadenectomy, in which the surgeon removes the adjacent lymph nodes

Few lifestyle modifications beyond those to decrease the risk for recurrent or other cancers, are necessary for people who have endoscopic resections. Partial gastrectomy requires moderate changes in diet and EATING HABITS to accommodate the reduced size of the stomach, primarily a shift to eating smaller meals more frequently and reducing the amount of carbohydrates in the diet. Total gastrectomy requires significant modifications in eating habits as the surgery connects the lower end of the ESOPHAGUS to the start of the DUODENUM, leaving no reservoir for ingested food. Most people can eat only a few bites of food at a time after total gastrectomy, making eating enough to meet the body's nutritional needs a fairly continuous process. As well, because the stomach produces the substances that make it possible for the body to absorb vitamins such as vitamin B₁₂, people who undergo total gastrectomy need NUTRITIONAL SUPPLEMENTS.

The outlook for stage 0 stomach cancer is excellent, with a 90 percent of people who undergo surgery reaching the five-year survival mark. The outlook remains very good for stage 1 stomach

cancer, with about a 70 percent five-year survival rate. More advanced stages of stomach cancer, in which the cancer spreads to involve other tissues and organs, remain difficult to treat successfully. Clinical research studies may offer the opportunity to participate in investigational treatments that extend life as well as improve QUALITY OF LIFE.

Risk Factors and Preventive Measures

As is the case with many kinds of cancer, age is the most significant risk factor. Most stomach cancers occur in people over age 60. Family history of stomach cancer or COLORECTAL CANCER (which is also an ADENOCARCINOMA of the gastrointestinal tract), long-term cigarette smoking (particularly in combination with excessive alcohol consumption) and OBESITY also raise the risk for stomach cancer. The most valuable preventive measure is FOBT to screen for the presence of blood in the gastrointestinal tract. Bleeding raises suspicion for several kinds of cancer that are highly treatable with early detection and intervention. People who have peptic ulcer disease should be tested and treated for *H. pylori* infection. A diet high in vegetables and low in smoked or preserved foods seems to lower the risk for stomach cancer.

See also ADENOCARCINOMA; ADENOMA-TO-ADENOCARCINOMA TRANSITION; CANCER RISK FACTORS; CANCER PREVENTION; CANCER TREATMENT OPTIONS AND DECISIONS; END OF LIFE CONCERNS; INFLAMMATORY BOWEL DISEASE (IBD); INTESTINAL POLYP; [LIVER CANCER](#); LYMPHEDEMA; PANCREATIC CANCER; SMOKING AND CANCER; [STAGING AND GRADING OF CANCER](#); SURGERY BENEFIT AND RISK ASSESSMENT.

toxic megacolon A serious condition in which a loss of **MUSCLE** tone in the lower **COLON** (typically the sigmoid colon) causes the preceding segment of colon to greatly enlarge (dilate). Air accumulates in the dilated bowel, increasing the pressure. Without prompt treatment intestinal perforation (rupture) is highly likely, with consequential **PERITONITIS**.

Toxic megacolon is a potentially life-threatening condition that requires emergency medical treatment and often surgery.

Toxic megacolon is usually a complication of inflammatory conditions affecting the gastrointestinal tract, such as **INFLAMMATORY BOWEL DISEASE** (**IBD**) or **INFECTION** (**COLITIS**). The congenital disorder **HIRSCHSPRUNG'S DISEASE**, in which the lower colon lacks nerves, can cause toxic megacolon in a newborn infant.

Symptoms and Diagnostic Path

A person who has toxic megacolon is very sick. Usually there is **FEVER** along with **ABDOMINAL DISTENTION**, rigidity, and **PAIN**. **REBOUND TENDERNESS** and absence of **BOWEL SOUNDS** are common findings. The person may be in **SEPTICEMIA** (septic shock), indicating **PERITONITIS**. The doctor often can make the diagnosis with an abdominal **X-RAY** that shows the dilated colon.

Treatment Options and Outlook

ANTIBIOTIC MEDICATIONS, **CORTICOSTEROID MEDICATIONS**, depending on the cause of the condition, and intravenous fluids to counter **DEHYDRATION** may help stabilize the colon, in combination with positional changes to attempt to move air (intestinal

gas) out of the bowel to help relieve the distention. Surgery to remove the dilated segment of bowel (colectomy) is often the only treatment to prevent or treat bowel perforation. The surgeon then connects the two healthy ends of bowel together to restore normal bowel function. With prompt and appropriate treatment, many people make a full recovery from toxic megacolon. However, it does present a serious challenge to the body's **HEALING** abilities. As well, any underlying conditions that precipitated the bowel dilation may continue to cause symptoms.

Risk Factors and Preventive Measures

The primary risk factor for toxic megacolon is any condition that causes **INFLAMMATION** of the colon. Taking medications to slow gastric motility (such as to treat **DIARRHEA**) may contribute to the circumstances resulting in toxic megacolon. Anyone who has colitis, **GASTROENTERITIS**, **DIVERTICULAR DISEASE**, **CELIAC DISEASE**, **IBD**, or other inflammatory condition affecting the gastrointestinal tract who experiences symptoms that could suggest toxic megacolon should see a doctor without delay.

See also **ILEUS**; **SHORT BOWEL SYNDROME**.

tube feeding See **ENTERAL NUTRITION**.

ulcer See **PEPTIC ULCER DISEASE**.

ulcerative colitis See **INFLAMMATORY BOWEL DISEASE** (**IBD**).

virtual colonoscopy See **COLONOSCOPY**.

vomiting The forceful expulsion of contents from the **STOMACH**, also called emesis. The force of vomiting may also draw digestive material from

the DUODENUM (first section of the SMALL INTESTINE). Like sneezing and coughing, vomiting is a protective and reflexive mechanism to rid the body of substances that threaten its well-being.

Vomiting occurs in response to NERVE impulses from the BRAIN's emesis center (also called vomiting center). The emesis center receives input from numerous body systems, including the gastrointestinal tract, vestibular system (which regulates balance), and circulatory system, as well as from the chemoreceptor trigger zone, another region of the brain that receives signals from the body. PAIN signals, particularly those the vagus nerve conveys, also travel to the emesis center, which is why severe pain may result in NAUSEA (queasiness and the feeling of being about to vomit) and vomiting.

Other variables that influence the emesis center include sensory perceptions such as foul smells or disturbing sights (which activate the chemoreceptor zone), hormonal shifts (such as occur in pregnancy to cause MORNING SICKNESS), and signals from the gastrointestinal tract indicating chemical changes such as from the presence of INFECTION or INFLAMMATION. Nausea, the sensation of queasiness and the urge to vomit, typically though not always precedes vomiting.

A complex series of physiologic events takes place to permit vomiting. Simultaneously the epiglottis closes (blocking the airway), the larynx lifts, and the upper esophageal sphincter opens. Then the DIAPHRAGM violently contracts, pulling it down and causing the open the lower esophageal sphincter to open, while the abdominal muscles contract with comparable force to push gastric (stomach) contents upward through the now open esophagus. Vomitus is highly acidic; chronic vomiting such as occurs with anorexia nervosa causes erosion of the tooth enamel. This material has a bitter taste and often leaves a burning sensation in the upper THROAT. Though the mechanism of vomiting is involuntary, there is some voluntary control over its initiation.

Episodic vomiting generally has no lasting consequences, though the very young and the very old can quickly become dehydrated. Vomiting that continues longer than three or four weeks without apparent cause requires medical evaluation. Treatment may include ANTIEMETIC MEDICATIONS,

dietary changes, or therapies to resolve underlying conditions. Complications of chronic or repeated vomiting may include ESOPHAGITIS, electrolyte imbalance, and ASPIRATION PNEUMONIA.

See also COUGH; CYCLIC VOMITING SYNDROME; DEHYDRATION; EATING DISORDERS; FOOD-BORNE ILLNESSES; LABYRINTHITIS; MÉNIÈRE'S DISEASE; SNEEZE.

Whipple's disease A bacterial INFECTION of the SMALL INTESTINE, also called intestinal lipodystrophy, that impairs absorption of fats (lipids). The PATHOGEN (infective BACTERIA) is *Tropheryma whippelii*. Though *T. whippelii* can infect various body systems including the HEART and the EYE, the gastrointestinal tract is its most common site. In the small intestine the bacteria create lesions (disruptions in the continuity of the intestinal mucosa) that destroy the villi, the microscopic, fingerlike extensions of tissue where much of the intestine's absorption functions take place. Researchers do not know how people acquire *T. whippelii*, though do know the infection can take years to decades to manifest symptoms.

Symptoms include DIARRHEA, GASTROINTESTINAL BLEEDING, OSTEOARTHRITIS, MALNUTRITION, unintended weight loss, HEADACHE, and FEVER. The diagnostic path may include general blood tests, BARIUM SWALLOW with small intestine flow-through, and ENDOSCOPY with biopsy to culture a tissue sample from the inner intestine. Treatment is a course of intravenous ANTIBIOTIC MEDICATIONS, typically penicillin and streptomycin or chloramphenicol in combination, with 12 to 18 months of oral antibiotic therapy to completely eradicate the bacteria.

See also GASTROENTERITIS; MALABSORPTION.

Zollinger-Ellison syndrome A rare disorder in which the STOMACH dramatically increases hydrochloric acid production, resulting in rampant PEPTIC ULCER DISEASE. Zollinger-Ellison syndrome develops as a consequence of benign tumors, called gastrinomas, that secrete the digestive HORMONE gastrin. Gastrin signals the stomach to produce acid, which the stomach continues doing as long as gastrin remains present. The excess acid that results causes extreme irritation of the gastric mucosa (stomach's lining), leading to numerous ulcers. The gastrinomas may form in the PANCREAS or the DUODENUM (first segment of SMALL INTESTINE).

Though gastrinomas are noncancerous, they often spread to other locations (notably the LIVER) and may develop into CANCER over time. Doctors do not know what causes Zollinger-Ellison syndrome though it appears to have a correlation with MULTIPLE ENDOCRINE NEOPLASIA (MEN) type 1, a disorder in which tumors (including gastrinomas) develop in numerous endocrine glands.

The symptoms of Zollinger-Ellison syndrome are the same as those for peptic ulcer disease (DYSPEPSIA, NAUSEA, sensation of fullness, possible GASTROINTESTINAL BLEEDING). ENDOSCOPY of the upper

gastrointestinal tract may reveal gastrinomas in the duodenum. Abdominal ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, OR MAGNETIC RESONANCE IMAGING (MRI) can detect gastrinomas in the pancreas or the duodenum. Treatment combines medication to reduce gastric acid production, such as H2 ANTAGONIST (BLOCKER) MEDICATIONS OR PROTON PUMP INHIBITOR (PPI) MEDICATIONS, and surgery to remove or reduce the gastrinomas when possible.

See also CANCER RISK FACTORS; CANCER PREVENTION; LIVER CANCER; PANCREATIC CANCER; PANCREATITIS; STOMACH CANCER.

THE ENDOCRINE SYSTEM

The endocrine glands produce hormones, chemical messengers that regulate many functions within the body. Physician specialists who treat endocrine conditions are endocrinologists and neuroendocrinologists. This section, “The Endocrine System,” presents a discussion of the endocrine glands and other structures, the hormones they produce and their functions, an overview of endocrine health and disorders, and entries about the health conditions that involve the endocrine system.

Structures of the Endocrine System

HYPOTHALAMUS	THYMUS
PITUITARY GLAND	ISLETS OF LANGERHANS
anterior pituitary lobe	ADRENAL GLANDS
posterior pituitary lobe	adrenal cortex
PINEAL GLAND	adrenal medulla
THYROID GLAND	OVARIES (female)
PARATHYROID GLANDS	TESTICLES (male)

Functions of the Endocrine System

The endocrine system and the NERVOUS SYSTEM work in tandem to direct and regulate the myriad functions of the body, the nervous system through electrical impulses that travel along the nerves and the endocrine system via chemical messengers called hormones. Endocrine glands, sometimes called ductless glands, produce hormones. The endocrine glands release their hormones directly into the bloodstream, and the bloodstream transports them to the cells. Cells throughout the body contain receptors for specific hormones, so even though hormones circulate freely through the blood they affect the functions of only the cells that have receptors for them.

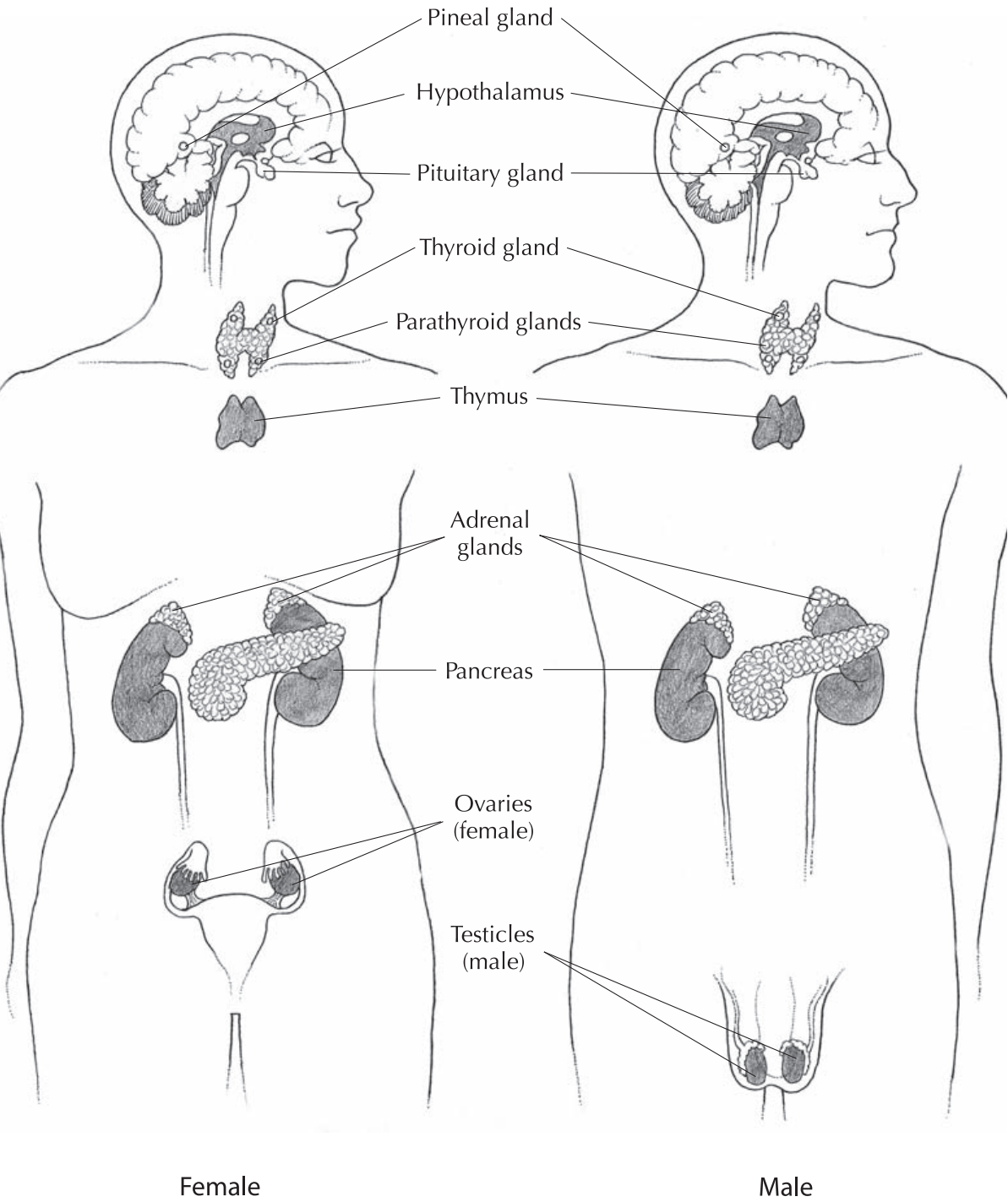
The endocrine glands may be clearly defined or loosely configured structures and are in numerous locations throughout the body. Some collections of endocrine cells inhabit other tissues and organs, such as those in the STOMACH and SMALL INTESTINE, and in the ISLETS OF LANGERHANS in the PANCREAS. Other endocrine cells form organized and independent structures, such as the ADRENAL GLANDS that cap the KIDNEYS and the THYROID GLAND which

lies across the front of the THROAT. Each endocrine structure produces specific hormones. Collectively the endocrine structures function in intimate synchronization and interaction with each other, continuously adjusting their secretions to accommodate the ever-changing conditions and needs of the body. An intricate matrix of cascades and feedback mechanisms allows this dynamic coordination to initiate and inhibit cellular activity.

THE MAJOR ENDOCRINE STRUCTURES AND THEIR HORMONES

Endocrine Structure	Primary Hormones
ADRENAL GLANDS	
adrenal cortex	ALDOSTERONE CORTISOL DEHYDROEPIANDROSTERONE (DHEA)
adrenal medulla	DOPAMINE EPINEPHRINE NOREPINEPHRINE
gastrointestinal tract	cholecystokinin (CCK) enterogastrone gastric inhibitive polypeptide (GPI) gastrin motilin secretin SOMATOSTATIN vasoactive intestinal peptide (VIP)
HYPOTHALAMUS	ANTIDIURETIC HORMONE (ADH) CORTICOTROPIN-RELEASING HORMONE (CRH)

The Endocrine System



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Endocrine Structure	Primary Hormones
HYPOTHALAMUS (continued)	dopamine GONADOTROPIN-RELEASING HORMONE (GNRH) GROWTH HORMONE-RELEASING HORMONE (GHRH) OXYTOCIN somatostatin THYROTROPIN-RELEASING HORMONE (TRH)
ISLETS OF LANGERHANS	GLUCAGON INSULIN somatostatin
KIDNEYS	ERYTHROPOIETIN (EPO) RENIN
ovaries	ESTROGENS INHIBIN PROGESTERONE
PARATHYROID GLANDS	PARATHYROID HORMONE
PINEAL GLAND	MELATONIN
PITUITARY GLAND	
anterior pituitary lobe	ADRENOCORTICOTROPIN HORMONE (ACTH) FOLLICLE-STIMULATING HORMONE (FSH) GROWTH HORMONE (GH) LUTEINIZING HORMONE (LH) PROLACTIN THYROID-STIMULATING HORMONE (TSH)
posterior pituitary lobe	stores and releases as needed: ADH oxytocin
PLACENTA	CHORIONIC GONADOTROPIN estrogen prolactin human placental lactogen (hPL) progesterone RELAXIN
testes	inhibin TESTOSTERONE
THYMUS	THYMOSIN

Endocrine Structure	Primary Hormones
THYROID GLAND	CALCITONIN THYROXINE (T ₄) TRIIODOTHYRONINE (T ₃)

Bridge between control systems: the hypothalamus The HYPOTHALAMUS is the structural and functional bridge between the BRAIN and the endocrine system. Composed primarily of brain tissue, it receives a constant barrage of NERVE signals from the thalamus, a structure of the brain that serves as a neurologic switchboard for sensory information related to sight, sound, touch, and taste. The physical transition from thalamus to hypothalamus is difficult to distinguish, highlighting the blurred line between neurologic and endocrine activity that gives rise to the subspecialty of medicine known as neuroendocrinology.

The functions of the hypothalamus primarily relate to survival. Through a combination of nerve impulses and hormonal signals, the hypothalamus regulates BLOOD PRESSURE, HEART RATE, gastrointestinal activity and digestion, body temperature, hunger, and thirst. Hypothalamic hormones target the PITUITARY GLAND, acting either to stimulate or inhibit (stop) the pituitary's secretions. The hypothalamus receives hormonal messages directly from the pituitary gland and indirectly through HORMONE levels in the BLOOD, one of a number of feedback mechanisms that helps regulate the hypothalamus's hormonal activity and maintain hormonal balance within the body.

Hormonal choreography: the pituitary gland Extending downward from the base of the hypothalamus, the pituitary gland bulbs out from the end of a short stalk. A dedicated capillary network, the hypophyseal portal circulation, circulates blood between the hypothalamus and the pituitary gland to fast track hormone delivery from the hypothalamus to the pituitary gland. A separate network of blood vessels supplies each structure with blood from the body's circulation to meet the metabolic needs of its cells and to carry pituitary hormones into the body. Communication between the pituitary gland and the hypothalamus is by necessity intimate and continuous, as the relationship between these two structures regulates basic bodily functions of survival.

The pituitary gland has two structural and functional divisions: the anterior lobe and the posterior lobe. The anterior pituitary lobe directs the activities of the thyroid, parathyroid, adrenal, and sex glands (gonads). The posterior pituitary lobe stores and secretes two hormones it receives from the hypothalamus: ANTIDIURETIC HORMONE (ADH), sometimes called vasopressin, and OXYTOCIN. The release of ADH directs the KIDNEYS to withhold more water, increasing blood volume and thus blood pressure. Oxytocin stimulates contractions of the UTERUS during CHILDBIRTH, and the mother's letdown REFLEX when BREASTFEEDING. Oxytocin also appears to play a role in sexual arousal in both women and men.

Recent research suggests oxytocin interacts with the limbic system, the intersection of neurologic and biochemical response to emotional stress. Levels of oxytocin in the bloodstream rise when stress hormone levels rise, leading researchers to speculate that oxytocin presents a counterbalance to the fight-or-flight response the stress hormones evoke by helping calm the body and restore homeostasis.

Stress management: the adrenal glands The adrenal glands drape across the tops of the kidneys. They produce an array of hormones that increase body functions in response to physiologic stress, such as heart rate and blood pressure. The two portions of the adrenal gland—the cortex (outer portion) and the medulla (inner portion)—have unique functions. The adrenal cortex, rind-like in appearance, secretes steroid hormones that it synthesizes from cholesterol. The primary adrenal cortex hormones are ALDOSTERONE and CORTISOL. Aldosterone regulates the fluid balance in the blood by directing the absorption of water and sodium in the kidneys. This is a fundamental component of a blood pressure–regulation mechanism called the RENIN-angiotensin-aldosterone (RAA) system. Cortisol has numerous effects related to metabolic functions throughout the body. The adrenal cortex also produces small amounts of estrogen, PROGESTERONE, and TESTOSTERONE in men and women alike.

The adrenal medulla, the core of the adrenal gland, secretes EPINEPHRINE, NOREPINEPHRINE (also called adrenaline and noradrenaline), and DOPAMINE. These hormones initiate rapid increases

in heart rate, respiration, and blood pressure, along with changes blood distribution, to allow the body to enter the classic fight-or-flight mode—the stress response. These hormones also provide the “adrenaline rush” that appeals to people who enjoy high-risk activities. Chemically these three substances are catecholamines. In the bloodstream the catecholamines are hormones regulating cell activity. In the interstitial (between-cell) fluid, they function as neurotransmitters, facilitating electrical impulses between nerves. The midbrain, including the hypothalamus, controls the adrenal medulla's secretory activity.

DOPAMINE “TRANSPLANT” FOR PARKINSON'S DISEASE

In the 1980s neurologists experimented with transplanting adrenal medullary tissue into the brains of people who had PARKINSON'S DISEASE, a progressively degenerative condition that results from depleted DOPAMINE in the BRAIN. Doctors hoped the adrenal medullary tissue would take root in the brain and continue to produce NOREPINEPHRINE, a precursor HORMONE to dopamine, which other brain chemicals would convert to much-needed dopamine. The risks of the procedure far outweighed the possible benefits, however, and failed to produce consistent results. Doctors today have largely abandoned the method.

Metabolic homeostasis: the thyroid gland

Spread across the throat like an elongated butterfly, the thyroid gland secretes the hormones THYROXINE (T₄) and TRIIODOTHYRONINE (T₃), which direct the rate at which cells consume energy. These hormones regulate numerous body functions, notably heart rate, digestive rate, and thermoregulation (body temperature, particularly response to cold). The thyroid's two lobes perform the same functions. The thyroid gland also secretes CALCITONIN, which acts to decrease calcium levels in the blood.

Thyroid hormones are essential for life. People who have HYPOTHYROIDISM (underactive thyroid gland) or who have had their thyroid glands destroyed or surgically removed must take lifelong thyroid hormone supplement or replacement therapy. Congenital thyroid deficiency, once called cretinism, in which the thyroid gland is missing or

dysfunctional in the unborn child, results in permanent damage to growth, development, and intellect. **HYPERTHYROIDISM**, in which the thyroid gland secretes excessive thyroid hormones, can cause serious and permanent damage to the heart and to the eyes (**GRAVES'S OPTHALMOPATHY**).

Calcium balance: the parathyroid glands Arising from the surface of the thyroid gland where it wraps around the **TRACHEA** are the four tiny **PARATHYROID GLANDS**, arranged in pairs on each of the thyroid gland's two lobes. Though each parathyroid gland alone is barely the size of a grain of rice, the parathyroid glands collectively keep the heart beating, the muscles moving, and the bones solid. The parathyroid glands produce **PARATHYROID HORMONE**, also called **parathormone**, which regulates the balance between calcium and phosphate. This equilibrium is essential for the conduction of nerve impulses in the heart and the skeletal muscles, proper growth of the bones and **TEETH** in childhood, and **BONE DENSITY** and **STRENGTH** in adulthood. The relationship between the thyroid gland and the parathyroid glands is functionally as well as physically intimate. The release of parathyroid hormone causes calcium levels in the blood to rise, counterbalancing the actions of **calcitonin**.

Glucose balance: the islets of Langerhans Distributed throughout the exocrine cells that make up the pancreas are about a million clusters of endocrine cells ranging in size from a few dozen to a few hundred cells. These clusters are the islets of Langerhans, and their three distinct cell types secrete the hormones **GLUCAGON**, **INSULIN**, and **SOMATOSTATIN**. These hormones regulate the body's balance and use of **GLUCOSE**, the primary source of fuel for many functions of **METABOLISM**. The islet cells also secrete a number of other hormones whose functions remain less clearly understood.

Reproduction: the gonads (sex glands) The gonads (sex glands)—the **OVARIES** in women and the **testes** in men—produce the hormones responsible for sexual maturity and reproductive capability. The gonads become active at **PUBERTY**, when the hypothalamus signals the pituitary gland to begin producing **FOLLICLE-STIMULATING HORMONE (FSH)** and **LUTEINIZING HORMONE (LH)**. These hormones in turn stimulate the gonads to produce the sex hormones. Men and women alike have all

of these hormones in their bodies; men have a predominance of testosterone and women have a predominance of estrogen and progesterone.

In women the ovaries produce estrogen, progesterone, and a small amount of testosterone. In men the testes produce testosterone, **INHIBIN** (which regulates **SPERM** production), and a small amount of estrogen along with a number of other minor hormones that have narrowly specialized functions. In men and women alike, the adrenal cortex produces small amounts of estrogen, progesterone, and testosterone. Estrogen is important for lipid metabolism and storage, testosterone is important for building and maintaining **MUSCLE** mass, and progesterone is an important precursor hormone for the synthesis of other steroid (lipid-based) hormones.

Building the immune system: the thymus In the 1940s doctors believed there was a connection between an enlarged **THYMUS** and sudden, unexplainable death in infants. They termed this condition status thymicolymphaticus and treated it with **RADIATION THERAPY** to destroy the thymus. There was little evidence to support this connection, however, and doctors began to notice that children treated with irradiation were unusually susceptible to infection. By the 1960s, as understanding began to grow about the functions of the immune system and researchers began to recognize the thymus had a role in immune function, and doctors abandoned both the concept of status thymicolymphaticus and its treatment.

The thymus secretes the hormone **THYMOSIN**, which helps the immune system's T-cell lymphocytes reach maturity and stimulates blood stem cell production in the **BONE MARROW**. Researchers speculate the thymus also produces several as yet unidentified hormones that influence immune function. Doctors now know, too, that the normal release of **GROWTH HORMONE (GH)** during the middle years of childhood stimulates an increase in the size of the thymus, explaining the reason for its enlargement in young children. During this period of development the thymus becomes particularly active in maturing and releasing into the body the T-cells that will form the foundation of immune function for the remainder of life.

Circadian cycles: the pineal gland The **PINEAL GLAND**, a small pinecone-shaped structure buried

deep in the brain, releases **MELATONIN**, a hormone associated with sleep cycles. Eastern traditions have long viewed the pineal gland as the metaphysical “third eye,” an energy pathway by which the brain communicates directly with the external environment. Western researchers are now discovering this perception may have tangible scientific substance. The pineal gland is located near the optic nerve, which appears to convey input about external light and dark to the pineal gland. Though researchers do not yet fully understand the mechanisms through which this occurs, they do know that melatonin secretion increases with darkness and decreases with lightness, apparently to facilitate the circadian cycle of sleep and wakefulness. Though as yet melatonin is the only identified hormone the pineal gland produces, researchers believe the pineal gland has additional functions and continue to study its role in the body.

Hormonal rhythms, cascades, and feedback loops The structures of the endocrine system function in tight synchronization with one another. Some hormonal processes are cyclic, under the control of the body’s circadian rhythm. Others are “on demand,” with physiologic events triggering the release of hormones.

For example, the hypothalamus releases **CORTICOTROPIN-RELEASING HORMONE (CRH)** on a regular cycle that begins a sharp spike a few hours before daybreak and peaks a few hours later, dropping off over the daylight hours to trough in the early evening. The release of CRH initiates a cascade of hormonal responses that accelerate metabolism in preparation for the body’s heightened level of activity during waking hours: CRH stimulates the pituitary gland to release **ADRENOCORTICOTROPIC HORMONE (ACTH)**, which subsequently stimulates the adrenal cortex to release cortisol. Cortisol then initiates numerous metabolic actions throughout the body.

Correspondingly, hormonal activity from the thyroid gland, islets of Langerhans, and gastrointestinal tract accelerates, instigating further cascades of hypothalamic-pituitary-adrenal activity. As the flow of CRH diminishes, the hormonal cascade slows. Feedback mechanisms also come into play. Cortisol reaches a certain level in the blood circulation, signaling the hypothalamus to stop

releasing CRH. The body’s metabolic activity begins to drop off. By nightfall the CRH level reaches its lowest point, and the body is metabolically ready for rest. The pineal gland’s release of melatonin similarly follows, and may in fact establish, the body’s circadian rhythm.

Other hormonal cycles follow different patterns. The hormonal cascades of puberty, for example, continue during the period of growth during which the secondary sex characteristics emerge—typically a range between the ages of 11 to 12 and 18 to 20. A woman’s **MENSTRUAL CYCLE** repeats approximately every 28 days. The hormones of **PREGNANCY** follow a precise schedule. Additional hormonal activity occurs in response to physiologic needs in integration with routine hormonal cycles. Feedback loops regulate such activity, with the endocrine system responding to stimuli from other body systems.

During intense physical exercise, for example, the hypothalamus releases ADH in response to hormonal signals from the kidneys (renin release) and barosensory signals from the cardiovascular system, stimulating the adrenal glands to release aldosterone, epinephrine, and norepinephrine to readjust fluid volume, electrolyte balance, heart rate, **BREATHING** rate, and blood pressure. The various physiologic changes that occur then signal the hypothalamus to stop releasing ADH. Such changes may take the form of rising levels of hormones in the blood or events that indicate the body’s needs are being met, such as increased blood volume and elevated blood pressure. Some hormones, such as ADH, are stimulatory; they initiate activity. Other hormones, such as somatostatin, are inhibitory; they stop activity.

Health and Disorders of the Endocrine System

Some endocrine structures are more active early in life, then recede to maintenance roles later in life. The thymus, for example, establishes the foundation of the immune system in early to middle childhood and subsequently shrinks in size and function at puberty to take a background, supportive role in immune function. Other endocrine structures become active at puberty such as the ovaries (female) or testes (male), known collectively as the gonads or sex glands. The sex glands establish the body’s **SECONDARY SEX-**

UAL CHARACTERISTICS and reproductive maturity. The functions of the sex glands taper with aging, most prominently in women to define the conclusion of FERTILITY (MENOPAUSE). Though men can remain fertile throughout their lives, testosterone levels begin to gradually diminish in the mid-30s. Still other endocrine tissues function only under special circumstances, such as the PLACENTA which secretes dozens of hormones that regulate pregnancy.

The most common endocrine disorder in the United States is DIABETES (known clinically as diabetes mellitus). Approximately 13 million Americans know they have diabetes, and health experts believe another 5 to 6 million more have diabetes though do not yet know, more than half of whom are over age 60. Diabetes is a significant health influence among adults as the leading cause of heart disease, kidney disease, blindness, and nerve damage (NEUROPATHY). Diabetes accounts directly for more than 70,000 lives lost each year, making it the sixth leading cause of death in the United States. Some people are able to manage their diabetes through lifestyle factors such as diet, exercise, and WEIGHT LOSS AND WEIGHT MANAGEMENT. Others must take medication such as oral antidiabetic medications or insulin injections. Type 1 diabetes is an autoimmune disorder in which the immune system attacks the islets of Langerhans, killing the cells that produce insulin. Type 2 diabetes typically develops in midlife or later, nearly always as a consequence of INSULIN RESISTANCE arising from lifestyle factors. Health experts believe most type 2 diabetes is preventable.

Also common is hypothyroidism (underactive thyroid). About 5 million Americans know they have hypothyroidism. Hypothyroidism affects numerous body functions, including heat regulation, heart rate, blood pressure, body weight, fertility, energy levels, and sleep quality. As with diabetes, health experts believe many more—perhaps another 10 million—have the condition and do not yet know. Hypothyroidism is more common among women and becomes more frequent with advancing age, with some health experts estimating as many as 20 percent of women over age 60 have the condition.

OBESITY, in which body weight due to excessive body fat is 20 percent or more greater than healthy

weight, is a complex confluence of endocrine, genetic, and lifestyle factors. Much research focuses on the role of hormones in body functions related to APPETITE (the desire to eat) and metabolism. Research in the 1990s identified two hormones, leptin and ghrelin, that strongly influence appetite. The stomach secretes ghrelin, and adipose (fat) cells throughout the body secrete leptin. The hypothalamus perceives the changing levels of these hormones in the bloodstream as signals of either hunger or satiety (sense of fullness), and correspondingly accelerates or decelerates digestion and metabolism (use of energy). This research holds intriguing implications, especially for type 2 diabetes. Doctors know that 90 percent of people who have type 2 diabetes also have obesity and estimate that a comparable percentage of people who have obesity also have either insulin resistance or diabetes. Health experts estimate obesity affects 15 percent of American children and 30 percent of American adults.

Traditions in Medical History

For centuries mystery shrouded the very existence of the endocrine glands and their functions. Until human autopsy (cutting open the body after death) became ethically and legally acceptable, doctors learned of endocrine glands or their functions only unintentionally. Physicians knew the signs consistent with the diseases of endocrine dysfunction but lacked the understanding of their causes and thus could not treat them. Historical records dating from ancient Mesopotamia, India, Greece, Rome, and China, for example, document the universal manifestation of diabetes, the first recognized, and even today the most common, endocrine disorder. In diabetes, the islets of Langerhans, collections of endocrine cells in the pancreas, stop secreting insulin, the hormone that “unlocks” cells to allow glucose (sugar), their primary fuel, to enter. As a result, glucose accumulates in the blood while cells literally starve to death.

Antiquarian healers diagnosed diabetes using the same concept modern doctors use (though with vastly different methods), testing the URINE for sugar. Because blood glucose levels rise with inadequate insulin presence, the kidneys attempt to restore the balance by extracting glucose from

the blood and passing it into the urine for excretion from the body. Though the modern method employs laboratory equipment that measures the amount of glucose present in the urine, the ancient physician relied on a far less sophisticated approach: An unfortunate assistant tasted the patient's urine, with sweetness confirming the diagnosis. More innovative or perhaps simply less influential healers had their patients urinate on the ground, then watched to see whether ants swarmed to the site. When ants were attracted to the urine, the diagnosis was "honey urine disease," known today as diabetes.

The diagnosis unfortunately offered little hope for treatment. Ancient healers knew honey urine was a harbinger of death but they did not understand the accountable disease mechanisms. Not until the early 20th century did the scientists Frederick Banting (1891–1941), Charles Best (1899–1978), and John James Rickard Macleod (1876–1935) discover insulin and correlate it to pancreatic function and diabetes. Their research ultimately demonstrated that regular injections of a purified solution prepared with ground pancreatic tissue from pigs or cows, which provided insulin, restored glucose metabolism in people who had diabetes.

The work earned the trio the 1923 Nobel Prize in Physiology or Medicine. More significant, it gave the prospect of normal life to countless people otherwise consigned to near-certain death. And it threw open the door to expanded knowledge of the role of the body's chemical messengers in health and in illness. Modern researchers hope to build on this knowledge to find a cure for diabetes, a disorder that despite treatment remains the leading cause of RENAL FAILURE and blindness and a significant cause of CARDIOVASCULAR DISEASE (CVD).

Breakthrough Research and Treatment Advances

The 20th century saw the field of endocrinology grow from the introduction of the term *hormone* in 1902 to amazing breakthroughs in understanding of, and treatments for disorders of, endocrine function and neuroendocrine interactions. Researchers now know of nearly 100 hormones the body produces and have developed synthetic hormones to replace or supplement the body's natural hormones as treatments for conditions such as diabetes, hypothyroidism, and osteoporosis. People who have insulin-dependent diabetes now take injections of insulin products genetically engineered in the laboratory to emulate human insulin's precise molecular structure, no longer dependent on purified extracts from animal tissues. Research exploring ISLET CELL TRANSPLANTATION shows promise for being among the therapies that might someday allow doctors to cure diabetes.

Researchers entered other frontiers of endocrine understanding as well. In 1935 scientists finally isolated and named testosterone, the male sex hormone. Shortly after came the discovery of estrogen, the female sex hormone. A quarter century later researchers had turned this knowledge into significant advances on both ends of the fertility spectrum, with the debut of the oral contraceptive (birth control pill) in 1960 and the birth of the first "test tube baby" in 1978. Both discoveries manipulate the hormones responsible for OVULATION, CONCEPTION, and pregnancy. Researchers also have come to recognize that hormones drive most primary cancers of the BREAST, uterus, PROSTATE GLAND, and testicles. New therapies use pharmaceutical interventions (synthetic hormones and chemicals that mimic the structure and action of hormones) to treat or prevent these cancers.



acromegaly A condition in which the PITUITARY GLAND secretes excessive GROWTH HORMONE (GH), causing the bones to thicken and become overgrown. This excessive growth is most apparent in the facial features and the extremities, especially the jaw, brow, hands, and feet. Most commonly acromegaly develops in midlife. When acromegaly occurs before the growth plates in the long bones of the arms and legs have fused, excessive height results. Doctors call this gigantism rather than acromegaly, though it is the same disease process. When excessive secretion of GH takes place after the growth plates have fused (generally after PUBERTY), the bones enlarge by thickening and spreading. This pattern of overgrowth results in the distortions characteristic of the disorder.

A BOND ACROSS TIME

Some medical historians believe the biblical giant Goliath and the sixteenth president of the United States, Abraham Lincoln (1809–1865), had in common the disorder of acromegaly. Both were exceedingly tall for the time in which they lived. Descriptions of Goliath and photographs of Lincoln suggest the characteristic features of acromegaly: overgrown facial features, excessive height, and unusually large hands and feet. Lincoln's headaches and fatigue, widely known, also were indications of acromegaly.

Though the small number of people doctors diagnose with acromegaly gives the perception this condition is rare, endocrinologists believe acromegaly is much more common than those numbers suggest. Acromegaly typically develops over years to decades, with symptoms emerging slowly and often nonspecifically. Many people learn they have acromegaly during evaluation for

other conditions that could account for their symptoms, such as HYPERTENSION (high BLOOD PRESSURE) or DIABETES.

The most common cause of acromegaly is an ADENOMA (noncancerous tumor) in the anterior lobe of the pituitary gland, increasing the quantity of cells that secrete GH. Occasionally an adenoma or, rarely, an ADENOCARCINOMA (an adenoma that has turned cancerous) that secretes GH and is located elsewhere in the body, such as the gastrointestinal tract (notably the PANCREAS) or the LUNGS, is responsible. Growth hormone does not itself cause growth but instead stimulates the LIVER and other structures to produce other hormones, known collectively as insulinlike growth factors, or IGFs (sometimes called somatotropin mediators or somatomedins), that increase the rate at which cells divide. The most prominent of these is INSULIN growth factor 1 (IGF-1). High GH secretion results in excessive IGF-1 circulating in the BLOOD, which becomes one of the clinical markers for making the diagnosis.

Symptoms and Diagnostic Path

Often the earliest symptoms of acromegaly are gradual changes in the hands and feet, especially swelling of the palms and soles. A person may need larger sizes of shoes or gloves than usual and find that rings or watches no longer fit. Other symptoms include

- frequent headaches and vision disturbances
- excessive sweating and body odor
- thickened, often darkened, SKIN and NAILS
- increasing space between the TEETH
- PAIN in the joints

- DYSMENORRHEA (abnormal MENSTRUATION) in women and ERECTILE DYSFUNCTION in men
- weakness and fatigue

Headaches and visual disturbances occur when the pituitary adenoma grows large enough to create pressure against structures of the BRAIN. Often this pressure affects the OPTIC NERVE, which passes near the pituitary gland, causing an array of vision disturbances. The excessive GH causes the SWEAT GLANDS to enlarge and increase production, causing the unpleasant body odor and excessive sweating. The overgrowth of BONE in the jaws displaces the teeth, often first apparent as a shift in bite (the way the teeth meet when chewing).

There are no definitive tests to diagnose acromegaly, requiring the endocrinologist to compile a picture of clinical and observational findings. About a third of people who have acromegaly have elevated GH levels in the blood an hour after they drink an oral GLUCOSE solution. Because of the constant interactivity between GH, insulin, and glucose, GH stays in the blood circulation for only a short time, and its levels vary widely in a healthy person. The level of IGF-1 is more indicative of excessive GH secretion because IGF-1 stays in the circulation for an extended time. However, IGF-1 levels naturally diminish with age and in conditions such as OBESITY and diabetes.

Because endocrine functions are so tightly integrated, often the endocrinologist will measure the blood levels of other hormones, such as those the THYROID GLAND, ADRENAL GLANDS, and sex glands produce. Other diagnostic procedures may include imaging studies such as X-rays to identify changes in bone structure and MAGNETIC RESONANCE IMAGING (MRI) to determine whether a pituitary adenoma is present. The endocrinologist also may ask to see photographs of the person taken over the preceding 5 to 10 years to evaluate changes in physical structure and appearance.

Treatment Options and Outlook

The optimal treatment is an OPERATION to remove the pituitary adenoma. The surgeon reaches the tumor from an incision made inside the NOSE, entering the brain from the nasal cavity (called transsphenoidal resection). Therapies such as

medications or radiation therapy may be necessary to shrink tumors larger than 10 centimeters (4 inches) or to treat tumors when surgery is not a viable option or cannot remove all of the tumor. In most people the surgery results in immediate relief of pressure-related symptoms such as HEADACHE and VISION IMPAIRMENT as well as a prompt return to normal levels of GH in the bloodstream. Many of the other symptoms then improve, though some of the changes the excessive GH has caused, such as bone overgrowth, remain.

MEDICATIONS TO TREAT ACROMEGALY

bromocriptine (Parlodel)

octreotide (Sandostatin)

pegvisomant (Somavert)

About a third of people who develop acromegaly also develop hypertension, resulting from the altered hormonal environment in the body, and HEART FAILURE, a consequence of the enlargement of the HEART in response to the excessive GH. Many also develop chronic OSTEOARTHRITIS, resulting from the overgrowth of CARTILAGE at the bone ends and the joints, and peripheral NEUROPATHY, resulting from overgrown tissues compressing the nerves. Often, these problems are what cause people to seek medical attention.

In health the interactions among GH, insulin, and SOMATOSTATIN regulate the hormonal balance that allows appropriate growth. In acromegaly, the excessive GH throws the equilibrium of this matrix out of kilter. As a result, people who have acromegaly are also likely to develop type 2 diabetes as a consequence of hormonal disturbances within the insulin–glucagon–somatostatin matrix. Diabetes and other consequential conditions may require ongoing therapy even after treatment for the acromegaly restores normal GH secretion. People who have acromegaly have an increased risk for developing COLORECTAL CANCER, which arises from adenomas of the intestinal wall (intestinal polyps).

Risk Factors and Preventive Measures

There are no known risk factors or preventive measures for acromegaly. Early diagnosis provides

the ideal opportunity to remove or suppress the responsible tumor.

See also ADENOMA-TO-CARCINOMA TRANSITION; HORMONE; HYPERHIDROSIS; [INTESTINAL POLYP](#).

Addison's disease Damage to or progressive failure of the adrenal cortex of the ADRENAL GLANDS, resulting in insufficient production of the hormones CORTISOL and ALDOSTERONE. The most common cause of Addison's disease, also called primary ADRENAL INSUFFICIENCY, is autoimmune, in which the IMMUNE SYSTEM attacks the cells of the adrenal cortex. Doctors do not know what precipitates such an attack. Other causes include events that can damage or destroy adrenal tissue such as INFECTION that infiltrates the adrenal gland tissue (notably TUBERCULOSIS), blunt trauma or other injury to the abdomen, and tumors. Because the body cannot make up for the lost function of the adrenal glands, treatment requires lifelong HORMONE THERAPY to provide adequate levels of cortisol and usually aldosterone as well. With treatment most people who have Addison's disease are able to enjoy normal lifestyles and activities, though must remain vigilant for indications of Addisonian crisis.

Addisonian Crisis (Adrenal Crisis)

Addisonian crisis, also called adrenal crisis, occurs when physical stress such as injury, infection, or illness increases the body's demand for cortisol beyond the capacity of the adrenal glands to produce. The body exhibits signs of SHOCK and cardiovascular shock, including extreme HYPOTENSION (low BLOOD PRESSURE), DYSPNEA (shortness of breath or difficulty BREATHING), and erratic HEART RATE.

Addisonian crisis is a life-threatening event that requires immediate injection of hydrocortisone and emergency medical care.

Prompt and appropriate medical intervention (injected hydrocortisone and supportive measures to sustain cardiovascular function) can restore normal functions. However, Addisonian crisis can quickly turn fatal. People who have Addison's disease often carry emergency doses of injectable hydrocortisone, with instructions for dosage, and should wear identification of some sort (bracelet

or necklace) that identifies them as having Addison's disease so medical aid response can act promptly with the correct measures.

Symptoms and Diagnostic Path

One of the earliest, though nonspecific, symptoms of Addison's disease is craving salt and salty foods, which occurs because the aldosterone deficit allows the KIDNEYS to release excessive amounts of sodium into the URINE. Other symptoms also tend to be nonspecific and include

- fatigue and tiredness
- postural hypotension (drop in blood pressure when rising from a sitting position)
- loss of APPETITE and weight loss
- MUSCLE weakness
- hyperpigmentation (darkening of the SKIN)
- irritability
- irregular MENSTRUATION (women)

The diagnostic path includes blood tests to measure the amounts of potassium, sodium, GLUCOSE, cortisol, and ADRENOCORTICOTROPIC HORMONE (ACTH). Other tests typically include a cortisol challenge—ACTH stimulation and CORTICOTROPIN-RELEASING HORMONE (CRH) stimulation tests—to assess the body's ability to produce cortisol and diagnostic imaging procedures such as MAGNETIC RESONANCE IMAGING (MRI) to visualize the hypothalamus, pituitary gland, or adrenal glands.

DISTINGUISHING FEATURES OF ADDISON'S DISEASE AND ADRENAL INSUFFICIENCY

Addison's Disease	Adrenal Insufficiency
normal ADRENOCORTICOTROPIC HORMONE (ACTH)	low ACTH
areas of HYPERPIGMENTATION	normal SKIN color
elevated BLOOD potassium level (HYPERKALEMIA)	normal blood potassium level
low blood sodium level (HYPONATREMIA)	normal blood sodium level
low blood GLUCOSE level (HYPOGLYCEMIA)	normal blood glucose level
deficient ALDOSTERONE production	normal aldosterone production

It is essential for the endocrinologist to distinguish between Addison's disease, which is primary adrenal insufficiency (the dysfunction originates with the adrenal cortex) and secondary adrenal insufficiency (the dysfunction arises from inadequate ACTH, or less commonly from inadequate CRH). Diagnostic test results make this distinction clear.

Treatment Options and Outlook

Treatment consists of medications (HORMONE therapy) to supplement or replace the adrenal hormones. Endocrinologists commonly prescribe oral hydrocortisone to supplement cortisol and fludrocortisone to supplement aldosterone. Medication dosages may change over time, and lifelong treatment is necessary. Circumstances that stress the body require additional medication, preferably in advance of the stress, when possible, to avert an Addisonian crisis. These circumstances include PREGNANCY, labor and delivery, surgery, and serious illness or injury.

Risk Factors and Preventive Measures

People who have other AUTOIMMUNE DISORDERS such as HYPOTHYROIDISM or type 1 DIABETES have an increased likelihood of developing the autoimmune form of Addison's disease. About 70 percent of people who have Addison's disease have the autoimmune form. There are no known preventive measures for Addison's disease.

See also CHRONIC FATIGUE SYNDROME; POLYGLANDULAR DEFICIENCY SYNDROME; STRESS AND STRESS MANAGEMENT; STRESS RESPONSE HORMONAL CASCADE.

adenoma A noncancerous tumor arising from epithelial cells that typically forms within glandular tissues or structures. An adenoma contains the same cells as the gland from which it arises, causing it to secrete the same hormones. The result is an excess of the HORMONE within the BLOOD circulation, which disrupts the endocrine balance to cause an array of symptoms specific to the hormone and its influences. Adenoma is a common cause of many acquired endocrine disorders and is usually treatable with surgery, medication, or RADIATION THERAPY. Adenomas that do not cause symptoms (asymptomatic) are exceedingly common, and researchers estimate as many as 35 percent of people have them.

The diagnostic path includes blood tests to measure blood levels of the hormone and imaging procedures to identify the adenoma's location. Because of the risk for an adenoma to become cancerous, endocrinologists prefer to surgically remove adenomas that cause symptoms. The surgery can be straightforward or complex, depending on the adenoma's location. In some circumstances the surgeon may need to remove the entire affected gland to remove the tumor, or may be unable to remove all of the adenoma. Either circumstance may make it necessary for the person to take long-term HORMONE THERAPY (with removal of the entire gland) or to take medication to suppress the tumor's activity. Endocrinologists often prefer to take a course of watchful waiting with asymptomatic adenomas rather than initiating any treatment.

See also ADENOMA-TO-CARCINOMA TRANSITION; INTESTINAL POLYP.

adrenal glands A pair of endocrine glands, sometimes called suprarenal glands, located one above each kidney. The right adrenal gland is clearly triangular in shape, and the left adrenal gland has more of a crescent shape. Pumpkin colored, each adrenal gland is about three inches long and two inches deep, and rises above the kidney one-half inch (left adrenal gland) to three-quarters inch (right adrenal gland). These differences are due to the asymmetrical placement of the KIDNEYS, with the left kidney placed higher than the right in the abdomen.

The adrenal gland consists of two structurally distinct divisions: the outer cortex and the inner medulla. The adrenal cortex, a thick rindlike structure that makes up about 90 percent of the adrenal gland structure, encloses the adrenal medulla. The adrenal cortex produces the steroid hormones ALDOSTERONE and CORTISOL, as well as ESTROGENS, PROGESTERONE, and TESTOSTERONE. The fibrous, soft inner structure of the adrenal gland, the adrenal medulla, secretes the peptide hormones DOPAMINE, EPINEPHRINE, and NOREPINEPHRINE.

The most familiar function of the adrenal glands is their management of the body's physiologic responses to stress, commonly identified as the fight-or-flight reaction. In response to NERVE and hormonal signals from the HYPOTHALAMUS, the

adrenal glands can flood cortisol, epinephrine, and norepinephrine into the BLOOD circulation. On a mundane basis the adrenal glands also broadly regulate myriad functions of survival, such as BLOOD PRESSURE and HEART RATE, continuously adjusting the levels of these hormones in the bloodstream to meet the body's daily needs.

ADRENAL HORMONES
Adrenal cortex
ALDOSTERONE
CORTISOL
ESTROGENS
PROGESTERONE
TESTOSTERONE
Adrenal medulla
DOPAMINE
EPINEPHRINE
NOREPINEPHRINE

The Adrenal Cortex

The primary hormones of the adrenal cortex—aldosterone and cortisol—regulate many functions necessary for survival. Cortisol directs numerous chemical interactions that facilitate GLUCOSE balance and are integral for carbohydrate and fat METABOLISM. Aldosterone regulates the sodium–potassium balance, maintaining appropriate blood volume and blood pressure. The adrenal cortex arises from the same tissue in the EMBRYO as the sex glands (OVARIES and TESTES) and retains a functional connection to them in that it also synthesizes and secretes estrogen, progesterone, and testosterone in males and females alike. These hormones have numerous roles in functions other than those of reproduction. Testosterone helps maintain MUSCLE mass and BONE DENSITY; estrogen is essential for cholesterol metabolism; and the adrenal cortex needs progesterone to synthesize aldosterone.

The adrenal gland has three distinct layers, or zones, each of which exclusively produces specific hormones. These zones are

- The zona glomerulosa, the outermost zone, synthesizes and secretes aldosterone under the regulation of ADRENOCORTICOTROPIC HORMONE (ACTH) and the enzyme angiotensin II (synthesized when the kidneys release RENIN).

- The zona fasciculata, the middle zone, synthesizes and secretes cortisol under the regulation of ACTH.
- The zona reticularis, the innermost zone, synthesizes and secretes sex hormones (estrogen, progesterone, and testosterone) under the primary regulation of ACTH with secondary influence from FOLLICLE-STIMULATING HORMONE (FSH) and LEUTEINIZING HORMONE (LH).

The Adrenal Medulla

The adrenal medulla develops from the same tissue as the NERVOUS SYSTEM and remains under neurologic control. The adrenal medulla produces the hormones dopamine, epinephrine (also called adrenaline), and norepinephrine (also called norepinephrine). These function in the body as hormones, facilitating chemical interactions among cells, and as neurotransmitters, facilitating the passage of nerve signals. The interactions occur within the adrenal gland as well; the adrenal medulla needs cortisol to synthesize epinephrine.

BODY AND BRAIN: SAME CHEMICALS, DIFFERENT CONCENTRATIONS

The adrenal medullary hormones DOPAMINE, EPINEPHRINE, and NOREPINEPHRINE are the same chemical composition as their NEUROTRANSMITTER counterparts in the BRAIN. However, the brain requires much higher concentrations of these substances than the body can tolerate. A protective mechanism called the BLOOD–BRAIN BARRIER, a membranous layer of cells in the BLOOD vessels of the brain, regulates the size of molecules that can enter and leave the brain's circulation. The molecules of these hormones are too large to pass through, keeping the body (central) and brain supplies of them separate.

Kidney Disease and Adrenal Function

RENAL FAILURE, RENAL CANCER, and KIDNEY TRANSPLANTATION may affect various aspects of adrenal function. When the kidneys fail, they stop producing the hormone renin, which is essential for blood pressure regulation within the renin–angiotensin–aldosterone (RAA) system. The kidneys release renin when blood volume drops as a hormonal signal to the adrenal cortex to release

aldosterone. Some people experience disruptions of the RAA hormonal matrix after kidney transplantation because the transplanted kidney may be slow to become fully functional. When this occurs the person may need medications to help regulate blood pressure and sodium–potassium balance.

Though a separate structure, the adrenal gland is in direct contact with the surface of the kidney. One of the three arteries that delivers oxygenated blood to the adrenal gland branches from the renal ARTERY before the renal artery reaches the kidney. NEPHRECTOMY (surgical OPERATION to remove the kidney) can disturb this blood supply and damage the adrenal gland. The risk of this is highest with total nephrectomy, such as when removing a kidney that has completely failed or when radical nephrectomy (removal of the kidney, URETER, adrenal gland, and substantial surrounding tissue) is necessary to treat kidney cancer. Though most people can adapt to having only one adrenal gland just as they can adapt to having only a single kidney, the loss of both adrenal glands requires lifelong HORMONE THERAPY to replace adrenal hormones (primarily cortisol and aldosterone, the hormones of the adrenal cortex, as other structures in the body also synthesize the hormones the adrenal medulla produces).

Adrenal Gland Disorders

The most common disorder affecting the adrenal glands is ADENOMA, a noncancerous tumor that secretes excessive hormones of the division of the adrenal gland (cortex or medulla) from which it arises. Most commonly adrenal adenomas typically develop in the zona fasciculata of the adrenal cortex, causing excessive secretion of cortisol (CUSHING’S SYNDROME). Adenomas that develop in the zona glomerulosa cause excessive secretion of aldosterone (HYPERALDOSTERONISM). PHEOCHROMOCYTOMA, a tumor (usually noncancerous) that secretes epinephrine and norepinephrine, may form in the adrenal medulla.

For further discussion of the adrenal glands within the context of the endocrine system’s structure and function please see the overview section “The Endocrine System.”

See also ADENOMA-TO-CARCINOMA TRANSITION; AGING, ENDOCRINE CHANGES THAT OCCUR WITH.

adrenal insufficiency A condition, also called secondary adrenal insufficiency, in which the ADRENAL GLANDS fail to produce enough CORTISOL because there is not enough ADRENOCORTICOTROPIC HORMONE (ACTH) in the bloodstream. The cause may be damage to the PITUITARY GLAND that prevents it from synthesizing ACTH (such as a tumor), or extended therapy with CORTICOSTEROID MEDICATIONS (such as to treat some AUTOIMMUNE DISORDERS).

A tumor or its treatment may destroy the anterior lobe of the pituitary gland, preventing it from synthesizing ACTH. When this occurs permanent HORMONE THERAPY becomes necessary to maintain appropriate hormonal balance in the body, as the pituitary gland is the body’s only source for ACTH.

During corticosteroid therapy, the high level of circulating corticosteroid in the bloodstream signals the HYPOTHALAMUS that no further release of cortisol is necessary. This inhibits the release of CORTICOTROPIN-RELEASING HORMONE (CRH), so there is no signal to the pituitary gland to release ACTH. In such circumstances adrenal insufficiency is more likely to happen when the person abruptly stops taking a corticosteroid medication rather than tapering it, though it can occur whenever a person takes corticosteroids for longer than four weeks. Though the body nearly always returns to normal HORMONE production in time, it is often necessary for the person to take supplemental hormone therapy in the interim.

Symptoms and Diagnostic Path

The symptoms of adrenal insufficiency are similar to those of ADDISON’S DISEASE and include

- tiredness and fatigue
- HYPOTENSION (low BLOOD PRESSURE)
- loss of APPETITE and weight loss
- MUSCLE weakness
- irritability

CONDITIONS AFFECTING THE ADRENAL GLANDS

ADDISON’S DISEASE	adrenal ADENOMA
ADRENAL INSUFFICIENCY	CUSHING’S SYNDROME
HYPOALDOSTERONISM	PHEOCHROMOCYTOMA
POLYGLANDULAR DEFICIENCY SYNDROME	

A history of recent (within several months) corticosteroid therapy is a strong indicator for adrenal insufficiency. The diagnostic path includes tests to measure the levels of potassium, sodium, glucose, cortisol, and ACTH in the blood. Other procedures typically include ACTH- and CRH-stimulation tests to assess the body's ability to produce cortisol. The endocrinologist may conduct diagnostic imaging procedures such as MAGNETIC RESONANCE IMAGING (MRI) or COMPUTED TOMOGRAPHY (CT) SCAN to visualize and evaluate the pituitary gland and adrenal glands.

DISTINGUISHING FEATURES OF ADRENAL INSUFFICIENCY AND ADDISON'S DISEASE

Adrenal Insufficiency	Addison's Disease
low ACTH	normal ACTH
normal SKIN color	areas of hyperpigmentation
normal BLOOD potassium level	elevated blood potassium level (HYPERKALEMIA)
normal blood sodium level	low blood sodium level (HYPONATREMIA)
normal blood GLUCOSE level	low blood glucose level (HYPOGLYCEMIA)
normal ALDOSTERONE production	deficient aldosterone production

Treatment Options and Outlook

Treatment consists of medication (hormone therapy), typically oral hydrocortisone, to supplement adrenal production of cortisol until the pituitary gland returns to normal ACTH production. Most adrenal insufficiency resolves within a year of onset. When the cause of the adrenal insufficiency is permanent, such as damage to or destruction of the anterior lobe of the pituitary gland, permanent hormone therapy becomes necessary as well. During treatment it is important for the person to remain vigilant for signs of adrenal crisis, which requires emergency medical treatment. Circumstances that increase the risk for adrenal crisis include physiologic stress such as trauma, INFECTION, surgery, and PREGNANCY and CHILDBIRTH.

Risk Factors and Preventive Measures

The leading risk factor for adrenal insufficiency is corticosteroid therapy. The typical approach is to taper the corticosteroid DOSE gradually, to allow the body's normal hormonal mechanisms to

resume. Abruptly stopping a corticosteroid medication after taking it for four weeks or longer greatly increases the risk for adrenal insufficiency.

See also CHRONIC FATIGUE SYNDROME; POLYGLANDULAR DEFICIENCY SYNDROME; STRESS AND STRESS MANAGEMENT.

adrenocorticotrophic hormone (ACTH) A peptide HORMONE, also called corticotropin, the anterior lobe of the PITUITARY GLAND produces to stimulate the adrenal cortex of the ADRENAL GLANDS to synthesize and release CORTISOL. ACTH is one of the hormones in the STRESS RESPONSE HORMONAL CASCADE. The HYPOTHALAMUS releases the hormone CORTICOTROPIN-RELEASING HORMONE (CRH) to stimulate the pituitary's synthesis of ACTH. When cortisol levels reach the appropriate level in the bloodstream the hypothalamus shuts down its release of CRH and the pituitary gland subsequently ceases ACTH production until cortisol levels again drop. This cycle is ongoing as cortisol has numerous actions within the body, notably to facilitate carbohydrate and fat METABOLISM and suppress INFLAMMATION and other aspects of the IMMUNE RESPONSE.

For further discussion of ACTH within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ALDOSTERONE; FOLLICLE-STIMULATING HORMONE (FSH); GROWTH HORMONE (GH); LUTEINIZING HORMONE (LH); PROLACTIN; THYROID-STIMULATING HORMONE (TSH).

aging, endocrine changes that occur with The endocrine system initiates many of the significant changes that mark the phases of life, from CONCEPTION to old age. Because critical endocrine processes slow with advancing age, many people believe the endocrine system holds the secrets to aging and thus the answers to slowing or preventing the changes that occur in the body that cause aging.

The most obvious endocrine changes that occur with age are those that regulate sexual maturation and reproduction. The onset of PUBERTY heralds the transition from childhood to adulthood and nearly every ENDOCRINE GLAND plays a role. The HYPOTHALAMUS steps up production and secretion of GONADOTROPIN-RELEASING HORMONE (GNRH), GROWTH

HORMONE—RELEASING HORMONE (GHRH), and THYROID—RELEASING HORMONE (TRH), initiating the hormonal cascades that generate tremendous growth spurts as well as the development of the secondary sex characteristics. The PITUITARY GLAND responds with accelerated secretion of FOLLICLE-STIMULATING HORMONE (FSH), GROWTH HORMONE (GH), LUTEINIZING HORMONE, AND THYROID-STIMULATING HORMONE (TSH) which in turn stimulate the gonads (OVARIES in females and TESTES in males) and affect METABOLISM in cells throughout the body. Surges in the sex hormones—ESTROGENS, PROGESTERONE, and TESTOSTERONE—complete the metamorphosis.

The hormonal changes that take place during PREGNANCY are among the most profound the human body experiences. The PLACENTA, the developing fetus's lifeline, produces dozens of hormones otherwise not found in the body. These hormones, coupled with hormonal changes in the woman's body, sustain the woman's body as a supportive environment for the unborn child and prepare it for further support (lactation) after birth. The hormones of pregnancy allow the muscles and ligaments of the abdomen to soften stretch to accommodate the enlarging UTERUS, increase the woman's BLOOD supply and metabolism (including thyroid hormones and INSULIN production), and increase vital functions such as BLOOD PRESSURE and HEART RATE.

Over the subsequent four or so decades the reproductive hormonal cascades slow. By midlife women end FERTILITY and enter MENOPAUSE, the cessation of MENSTRUATION and OVULATION. Rapid drops in estrogen and progesterone elicit major changes in a woman's body. The changes in men are less dramatic though nonetheless apparent. Testosterone levels peak around age 22 and steadily decline, tapering by age 60 to about 50 percent of peak levels. Men notice redistribution of body fat, decreased MUSCLE mass, and thinning scalp HAIR.

Also with advancing age levels of the hormones of the adrenal cortex, particularly cortisol, begin to decline. This affects body functions ranging from blood pressure and heart rate to immune response and GLUCOSE metabolism. These changes are among the changes some researchers believe hold the key to slowing, halting, or even reversing some of the events and consequences of aging. Accompanying these and other endocrine changes

that occur with advancing age are increased risks for numerous health conditions such as CARDIOVASCULAR DISEASE (CVD), DIABETES, LIVER disease, and kidney disease. Nearly all hormonal production and endocrine processes diminish by age 80, and the body itself slows.

See also ANTI-AGING APPROACHES; LIFE EXPECTANCY; LIFESTYLE AND HEALTH.

aldosterone A steroid HORMONE the adrenal cortex of the ADRENAL GLANDS produces that plays a key role in regulating BLOOD PRESSURE. Aldosterone is vital for life; the body can sustain its functions for only a few days without it. Chemically aldosterone is a mineralocorticosteroid, a type of steroid (cholesterol-based structure) that influences the body's balance of minerals such as sodium and potassium. Aldosterone targets cells in the KIDNEYS that regulate the amounts of these minerals which remain in the bloodstream. The adrenal cortex releases aldosterone when the amount of potassium in the BLOOD increases or when the kidneys release the hormone RENIN in response to decreased blood volume flowing through the kidneys. Renin initiates a series of enzyme conversions that result in the production of angiotensin II, which then stimulates aldosterone production in the adrenal cortex.

LICORICE AND ALDOSTERONE

Long-term, excessive consumption of natural licorice (*Glycyrrhiza glabra* extract or glycyrrhizic acid) interferes with aldosterone binding and allows aldosterone levels in the BLOOD to rise, establishing symptoms similar to those HYPERALDOSTERONISM. Doctors call the resulting condition pseudo-hyperaldosteronism. Most licorice-flavored candies and other products in the United States do not contain natural licorice. However, natural licorice is an ingredient in many products in other countries, notably in Europe.

The release of aldosterone increases sodium retention in the blood and potassium excretion into the URINE, raising levels of sodium and dropping the levels of potassium in the blood. The higher sodium level correspondingly draws more water into the blood, increasing the blood volume.

Aldosterone also acts on the peripheral arterioles, the tiny arteries within the tissues, causing them to constrict. The combined effect of increased blood volume and peripheral vasoconstriction causes blood pressure to rise. This is a fundamental cascade of one of the body's primary blood pressure-regulatory mechanisms, the renin-angiotensin-aldosterone (RAA) system. Some medications to treat congestive HEART FAILURE and HYPERTENSION (high blood pressure) work by blocking the action of aldosterone.

Aldosterone deficiency, such as may result with ADRENAL INSUFFICIENCY and ADDISON'S DISEASE, causes HYPOTENSION (low blood pressure) and electrolyte imbalances that can cause ARRHYTHMIA (disturbance of the HEART'S rhythm and rate). Untreated aldosterone deficiency is fatal. Treatment with hormone-replacement therapy restores homeostasis. Excessive aldosterone in the bloodstream (HYPERALDOSTERONISM) typically results from an adrenal ADENOMA (noncancerous tumor) arising from the middle section of the adrenal cortex, the zona fasciculata, which produces aldosterone.

For further discussion of aldosterone within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ADRENOCORTICOTROPIC HORMONE (ACTH); CORTICOTROPIN-RELEASING HORMONE (CRH); CORTISOL; DOPAMINE; EPINEPHRINE; NOREPINEPHRINE.

amyloidosis An uncommon and potentially fatal disorder of METABOLISM in which the BONE MARROW produces defective antibodies that result in an abnormal protein, amyloid. The amyloid leaves the bone marrow in the BLOOD and forms fibrous deposits in organs and tissues throughout the body. The deposits interfere with normal functions, which can result in severe damage to and failure of organs such as the HEART, LIVER, and KIDNEYS. Amyloid deposits can also accumulate in the nerves and NERVOUS SYSTEM, LYMPH NODES, and blood vessels. There are three forms of amyloidosis: primary, secondary, and hereditary.

Primary amyloidosis Primary amyloidosis, also called idiopathic amyloidosis, occurs independently of other disease processes and without known cause (idiopathic). Most people who have

amyloidosis have this form, which tends to affect the heart, LUNGS, THYROID GLAND, liver, intestines, SKIN, and tongue.

Secondary amyloidosis Secondary amyloidosis accompanies or occurs as a consequence of other disease processes. The most common association is with MULTIPLE MYELOMA, a CANCER of the lymph system. About 15 percent of people who have multiple myeloma develop secondary amyloidosis. Secondary amyloidosis also may occur in conjunction with chronic inflammatory disorders such as RHEUMATOID ARTHRITIS or with chronic INFECTION such as TUBERCULOSIS and OSTEOMYELITIS. Secondary amyloidosis tends to affect the liver, SPLEEN, kidneys, ADRENAL GLANDS, and lymph nodes.

Hereditary amyloidosis Rarely, a person inherits amyloidosis as a result of genetic MUTATION. The amyloid deposits in hereditary amyloidosis are most likely to accumulate in the heart, kidneys, intestines, vitreous humor (the gelatinous substance inside the EYE), and PERIPHERAL NERVES.

Symptoms and Diagnostic Path

Symptoms of amyloidosis vary, depending on the organ systems affected. Many people experience generalized symptoms such as weakness, tiredness and fatigue, and unexplained weight loss. Other symptoms that may occur with amyloid deposits in specific organs or systems include

- DIARRHEA (gastrointestinal)
- tingling and numbness in the hands and feet (nerves)
- ARRHYTHMIA (irregularities in the heartbeat; heart)
- swollen tongue and difficulty swallowing (tongue; gastrointestinal; nerves)
- DYSPNEA (shortness of breath; lungs, heart)
- HEPATOMEGALY (enlarged liver; liver)

Amyloidosis also may manifest through symptoms of disease process such as HYPOTHYROIDISM (amyloid deposits in the thyroid gland) and kidney failure (amyloid deposits in the kidneys). The diagnostic path includes clinical assessment of symptoms, blood and URINE tests that may detect

the presence of abnormal proteins, and biopsy of representative amyloid deposits.

Treatment Options and Outlook

There is no curative treatment for amyloidosis. When amyloidosis is secondary, treatment for the underlying condition often mitigates the symptoms and progression of the amyloidosis. Treatment for primary amyloidosis targets symptom relief. In some people, a regimen of CHEMOTHERAPY halts the amyloidosis progression for up to several years. Kidney, heart, or liver transplantations are sometimes viable options when amyloid deposits accumulate in these organs. STEM CELL transplantation shows promise for long-term relief, though existing amyloid deposits remain in the tissues. Many people are able to control their symptoms for long periods of time through carefully selected therapeutic measures.

Risk Factors and Preventive Measures

There are no known risk factors or preventive measures for primary amyloidosis. Multiple myeloma and chronic inflammatory disorders and infections are significant risk factors for secondary amyloidosis. Amyloidosis is more likely to develop when these conditions are long-term and poorly controlled. Though it is not possible to prevent secondary amyloidosis, prompt and appropriate treatment for the underlying condition may mitigate its manifestation.

See also CHRONIC FATIGUE SYNDROME; FAMILIAL MEDITERRANEAN FEVER; INFLAMMATION; ORGAN TRANSPLANTATION; SARCOIDOSIS.

androgens A collective term for the “male” sex hormones, prohormones (chemical precursors the body converts to hormones), and metabolites (byproducts of HORMONE METABOLISM). Androgens are steroid hormones the body synthesizes from cholesterol; they are variably anabolic (they build MUSCLE mass, some more actively than others). Androgens are also the precursors (starting point) for the ESTROGENS (“female” sex hormones). The most abundant and familiar androgen is TESTOSTERONE. In addition to establishing male secondary sex characteristics and FERTILITY, androgens have multiple functions in men and women both with

regard to muscle mass and STRENGTH, BONE DENSITY, LIBIDO (sex drive), and metabolism.

Men and women alike have androgens (just as both sexes also have estrogens). The gonads, or sex glands (OVARIES in women and TESTES in men), synthesize (produce) most of the androgens in the BLOOD circulation. The adrenal cortex of the ADRENAL GLANDS and adipose (fat) cells also synthesize androgens. The HYPOTHALAMUS’s secretion of GONADOTROPIN-RELEASING HORMONE (GNRH) regulates the hormonal cascade for endogenous (within the body) androgen production and release. Some androgens are available as exogenous supplements used to treat disorders of androgen deficiency as well as taken illicitly to enhance athletic performance.

ENDOGENOUS ANDROGENS

androstane	androstenediol
androstenedione	androstrenolone
androsterone	DEHYDROEPIANDROSTERONE (DHEA)
dihydrotestosterone	TESTOSTERONE

See also ANABOLIC STEROIDS AND STEROID PRECURSORS; HIRSUTISM; HORMONE THERAPY; HYPOGONADISM; INFERTILITY; INSULIN RESISTANCE; POLYGLANDULAR DEFICIENCY SYNDROME; PROSTATE CANCER; SPERMATOGENESIS.

antidiuretic hormone (ADH) A peptide HORMONE, also called vasopressin, the HYPOTHALAMUS synthesizes (produces) and the posterior lobe of the PITUITARY GLAND stores and releases. ADH regulates the amount of water the KIDNEYS withhold in the bloodstream. The hypothalamus signals the pituitary gland to release ADH when the body needs additional fluid, such as during excessive sweating with heat or intense exercise. Increased ADH in the BLOOD causes the kidneys to withhold more water from the circulating blood, raising blood volume and decreasing URINE production. In high concentrations, ADH acts to constrict peripheral arterioles (the smallest arteries deep in the tissues). In combination, these effects are among the body’s mechanisms for regulating BLOOD PRESSURE. Dysfunction of the pituitary gland, and less commonly the hypothalamus, can result in inadequate levels of ADH in the bloodstream, causing the rare

condition DIABETES INSIPIDUS (which is not the same disease process as DIABETES mellitus, a disorder of INSULIN production or METABOLISM). Kidney disease may also interfere with the ability of the kidneys to respond to ADH.

For further discussion of ADH within the context of the endocrine system's structure and func-

tion please see the overview section "The Endocrine System."

See also ADRENOCORTICOTROPIN HORMONE (ACTH); ALDOSTERONE; FOLLICLE-STIMULATING HORMONE (FSH); GROWTH HORMONE (GH); LUTEINIZING HORMONE (LH); OXYTOCIN; PROLACTIN; RENIN; THYROID-STIMULATING HORMONE (TSH).



calcitonin A peptide HORMONE the THYROID GLAND produces that increases the amount of calcium the bones can accept. Calcitonin functions in synchronization with PARATHYROID HORMONE, which the PARATHYROID GLANDS secrete, to maintain calcium balance in the BLOOD and in the body. Calcium is essential for BONE DENSITY and STRENGTH, as well as for the conduction of NERVE impulses in MUSCLE tissue, including that of the HEART. The balance between calcitonin and parathyroid hormone maintains a constant level of calcium in the blood to allow proper nerve conduction for heart function as well as skeletal muscle function. This balance may come at the expense of the amount of calcium in the bones, however, which the body uses as a “bank” for the storage and withdrawal of calcium. Calcitonin facilitates calcium “deposit” to the bones by channeling calcium from the blood into the bones. It binds with receptor sites on the surfaces of osteoblasts, the cells within the bones that produce new BONE tissue.

A form of THYROID CANCER, medullary thyroid cancer, forms in the parafollicular cells that produce calcitonin. Excessive levels of calcitonin in the blood may indicate such a cancer. Disorders of the parathyroid glands that affect the secretion of parathyroid hormone may also disrupt the levels of calcitonin in the blood.

For further discussion of calcitonin within the context of the endocrine system’s structure and function, please see the overview section “The Endocrine System.”

See also OSTEOPOROSIS; THYROXINE (T₄); TRIIODOTHYRONINE (T₃).

cholecystokinin See DIGESTIVE HORMONES.

chorionic gonadotropin A peptide HORMONE of PREGNANCY that the fertilized ovum (egg) secretes to stimulate the corpus luteum to continue producing PROGESTERONE, which maintains an environment within the UTERUS to support the implantation of the EMBRYO. The corpus luteum, a temporary endocrine structure, develops in an ovarian follicle after the follicle releases an ovum, marking the start of OVULATION. The corpus luteum then begins secreting progesterone, which causes the lining of the uterus to thicken and its BLOOD supply to enrich in preparation for pregnancy. Without chorionic gonadotropin the corpus luteum deteriorates and the uterine lining sloughs away (MENSTRUATION). About eight weeks into pregnancy the PLACENTA forms and takes over chorionic gonadotropin production, which continues until birth. Pregnancy tests measure the amount of chorionic gonadotropin in the URINE or the blood. Fertility specialists use injections of chorionic gonadotropin (called human chorionic gonadotropin, or hCG, in its pharmaceutical form) to stimulate ovulation in women and TESTOSTERONE production, to encourage SPERM production, in men.

For further discussion of chorionic gonadotropin within the context of the endocrine system’s structure and function, please see the overview section “The Endocrine System.”

See also ANABOLIC STEROIDS AND STEROID PRECURSORS; CONCEPTION; ESTROGENS; FERTILITY; OXYTOCIN; PROLACTIN; RELAXIN.

corticotropin-releasing hormone (CRH) A peptide HORMONE the HYPOTHALAMUS synthesizes and releases in response to endocrine and neurologic signals that report the status of the body’s vital functions. CRH is one of the hormones in the

STRESS RESPONSE HORMONAL CASCADE and stimulates the anterior lobe of the PITUITARY GLAND to produce ADRENOCORTICOTROPIC HORMONE (ACTH). ACTH in turn stimulates the ADRENAL GLANDS to release CORTISOL, a steroid hormone that has numerous actions in the body. The level of cortisol in the bloodstream is one of the endocrine signals that determines the release of CRH. The hypothalamus also releases CRH in a rhythmic pattern that coincides with the body's circadian cycle of sleep and wake. CRH levels peak just before dawn and trough just before dusk, establishing higher ACTH and cortisol levels during the waking hours.

For further discussion of CRH within the context of the endocrine system's structure and function, please see the overview section "The Endocrine System."

See also GONADOTROPIN-RELEASING HORMONE (GNRH); GROWTH HORMONE-RELEASING HORMONE (GHRH); THYROTROPIN-RELEASING HORMONE (TRH).

cortisol A HORMONE the adrenal cortex of the ADRENAL GLANDS produces. Chemically cortisol is a glucocorticosteroid, a type of steroid (cholesterol-based structure) that influences carbohydrate and fat METABOLISM (GLUCOSE balance) in the body. Cortisol is the main player in the STRESS RESPONSE HORMONAL CASCADE, essential for activating other hormones and chemical processes required for many vital functions within the body. All cells in the body have receptors for cortisol. The body requires a minimum level of cortisol in the bloodstream, as well as increased amounts of cortisol to respond to stress by raising BLOOD PRESSURE, HEART RATE, BREATHING, and metabolic rate. Cortisol also counters the body's IMMUNE RESPONSE, helping to subdue areas of INFLAMMATION after they develop.

Cortisol levels fluctuate in a rhythmic pattern over the course of 24 hours, being highest during waking hours when the body is most active and lowest a few hours after falling asleep. To maintain this pattern the HYPOTHALAMUS initiates a cascade of hormonal activity by releasing CORTICOTROPIN-RELEASING HORMONE (CRH) in synchronization with the body's circadian rhythm (cycle of wake and sleep). CRH stimulates the anterior lobe of the PITUITARY GLAND to release ADRENOCORTICOTROPIC HORMONE (ACTH). ACTH in turn causes the adrenal cortex to produce and

release cortisol. When the BLOOD level of cortisol is adequate, the hypothalamus ceases release of CRH, the pituitary gland ends release of ACTH, and the adrenal cortex stops cortisol production. When the cortisol level in the blood drops or physiologic sensors (such as barosensors that detect changes in blood pressure) indicate a need to respond to stress the hypothalamus again boosts CRH output.

Cortisol production increases in response to physiologic stress such as intense physical exercise, as well as to emotional stress such as fear or anger. Research suggests that persistently elevated cortisol levels result in long-term damage to the cardiovascular system, notably contributing to HYPERTENSION (high blood pressure) and ARTERIOSCLEROSIS (stiffening of the arteries). Chronically insufficient levels of cortisol in the blood result in ADDISON'S DISEASE; chronically excessive levels of cortisol in the blood result in Cushing's syndrome. People who take long-term CORTICOSTEROID MEDICATIONS to treat chronic inflammatory conditions may develop acquired Cushing's syndrome, also called hyperadrenocorticism. Pharmaceutical preparations of cortisol commonly used as anti-inflammatory medications are cortisone and hydrocortisone.

For further discussion of cortisol within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ALDOSTERONE; DOPAMINE; EPINEPHRINE; NOREPINEPHRINE; STRESS AND STRESS MANAGEMENT; WORKPLACE STRESS.

Cushing's syndrome A constellation of symptoms that occur as a consequence of high levels of CORTISOL in the bloodstream. Cushing's syndrome may result from long-term CORTICOSTEROID MEDICATIONS (exogenous Cushing's syndrome) or from excessive cortisol production within the body (endogenous Cushing's syndrome). Untreated Cushing's syndrome affects many vital functions including BLOOD PRESSURE and HEART RATE, and can be fatal.

Exogenous Cushing's Syndrome

Exogenous Cushing's syndrome is the more common form of this condition and typically occurs in

people taking long-term corticosteroid therapy to suppress the IMMUNE RESPONSE such as following ORGAN TRANSPLANTATION (to prevent GRAFT VS. HOST DISEASE and organ rejection) or to treat chronic inflammatory conditions such as ASTHMA, SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), RHEUMATOID ARTHRITIS, SARCOIDOSIS, and INFLAMMATORY BOWEL DISEASE (IBD). Occasionally multiple corticosteroid injections into inflamed joints can also produce exogenous Cushing's syndrome.

Endogenous Cushing's Syndrome

Cushing's disease is an older term for endogenous Cushing's syndrome, which most commonly occurs as a result of adrenal or pituitary ADENOMA (noncancerous tumor) that increases cortisol secretion. A pituitary adenoma causes the anterior lobe of the PITUITARY GLAND to produce excessive ADRENOCORTICOTROPIC HORMONE (ACTH). The ACTH stimulates the adrenal cortex of the ADRENAL GLANDS to secrete cortisol. An adrenal adenoma develops in the adrenal cortex and itself secretes cortisol independent of ACTH stimulation.

Other causes of endogenous Cushing's syndrome include adrenal hypertrophy (enlargement of the adrenal glands), which increases cortisol secretion, and ACTH-secreting tumors located elsewhere in the body such as some cancers of the lung, PANCREAS, and BREAST. As with pituitary adenoma, the ACTH secretion stimulates the adrenal cortex to increase cortisol production. Cushing's syndrome is sometimes one of the earliest indications of small-cell LUNG CANCER (SCLC), the tumors of which are characteristically ACTH secreting.

Symptoms and Diagnostic Path

The symptoms and signs of Cushing's syndrome are the same regardless of the condition's cause and typically include

- a rounded, flushed face ("moon face")
- transition to an "apple" body shape: thickened trunk due to accumulated abdominal fat and thinned arms and legs due to MUSCLE atrophy (wasting)
- accumulation of fat in a "hump" between the shoulder blades
- HIRSUTISM (increased body HAIR) and ACNE

- HYPERTENSION (high blood pressure)
- delayed wound HEALING and decreased resistance to INFECTION
- irritability, DEPRESSION, mood swings, and difficulty concentrating

The diagnostic path begins with BLOOD and URINE tests to measure the body's levels and excretion of cortisol. When the endocrinologist suspects exogenous Cushing's syndrome due to corticosteroid therapy, these tests are often conclusive for the diagnosis. The endocrinologist may conduct additional tests to assess the body's response to dexamethasone (a corticosteroid) and ACTH (dexamethasone test and ACTH-stimulation test, respectively) when endogenous Cushing's syndrome is likely. Imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN OR MAGNETIC RESONANCE IMAGING (MRI) can reveal structural abnormalities, including tumors, of the pituitary gland and the adrenal glands.

Treatment Options and Outlook

Treatment targets reducing the amount of cortisol in the blood circulation. With exogenous Cushing's syndrome, treatment usually means transitioning to noncorticosteroid medications to manage the underlying condition and its symptoms. Treatment in endogenous Cushing's syndrome may be surgery to remove or RADIATION THERAPY to shrink a pituitary or adrenal adenoma, appropriate treatment for an ACTH-secreting tumor located elsewhere in the body, or medications such as ketoconazole or mitotane to suppress ACTH or cortisol synthesis. Some people require HORMONE THERAPY (sometimes long-term) to supplement or replace adrenal or pituitary hormones after treatments that target the gland directly.

Risk Factors and Preventive Measures

The primary risk factor for exogenous Cushing's syndrome is corticosteroid therapy. Transitioning to noncorticosteroid medications generally relieves Cushing's syndrome symptoms and often prevents the condition from developing. However, noncorticosteroid medications may have undesired side effects or be less effective in controlling the underlying condition for which the doctor prescribes

them. Endogenous Cushing's syndrome is not preventable though early diagnosis minimizes its consequences and affords a wider range of treatment.

See also [ADDISON'S DISEASE](#); [ADRENAL INSUFFICIENCY](#); [POLYCYSTIC OVARY SYNDROME \(PCOS\)](#); [POLYGLANDULAR DEFICIENCY SYNDROME](#).

dehydroepiandrosterone (DHEA) A precursor steroid HORMONE the adrenal cortex of the ADRENAL GLANDS synthesizes from cholesterol. The OVARIES or TESTES, and to a lesser extent the adrenal cortex, further formulate DHEA into TESTOSTERONE and ESTROGENS. LUTEINIZING HORMONE (LH) provides the hormonal stimulus for this synthesis. Levels of DHEA in the BLOOD circulation begin to rise around age 10, preceding the onset of PUBERTY, and peak in the mid-20s. DHEA levels in the bloodstream decline by about 15 percent a decade until about age 75, at which point the level stabilizes at about 15 percent of what it was at its peak 50 years earlier. Though there is speculation that diminishing DHEA levels may in some way precipitate the changes that take place with aging, researchers have yet to identify the mechanisms responsible.

See also ANABOLIC STEROIDS AND STEROID PRECURSORS; DHEA SUPPLEMENT.

diabetes A condition, clinically known as diabetes mellitus, in which the ISLETS OF LANGERHANS do not produce enough INSULIN or the body's cells do not appropriately respond to insulin, resulting in an inability of the cells to accept GLUCOSE. There are three major forms of diabetes: type 1, type 2, and gestational. Lifestyle factors significantly influence the development and course of diabetes, particularly type 2. Diabetes is the most common endocrine disorder.

Diabetes is a significant health concern in the United States, with more than 13 million people knowing they have the condition. Another 5 or 6 million have diabetes though are unaware. Diabetes is the sixth leading cause of death in the United States, directly claiming 70,000 lives each year. As a leading cause of CARDIOVASCULAR DISEASE

(CVD), kidney disease, and RENAL FAILURE, diabetes contributes to thousands more deaths as well. Diabetes is also the primary cause of VISION IMPAIRMENT and blindness, and a significant cause of peripheral NEUROPATHY (NERVE damage), among American adults.

Medical texts that are several thousand years old make reference to diabetes. Ancient physicians identified diabetes as the "honey URINE" disease, a moniker that became refined through the centuries to the somewhat less graphic "sugar diabetes." Until the discovery of insulin in the early 1920s, the diagnosis of diabetes was a death sentence. Efforts to manage the disease by restricting sugar were futile because the true problem was not too much sugar but rather not enough insulin.

As researchers and doctors gained greater understanding of diabetes, they realized it was insulin that made possible glucose's entry into the cells. Doctors now know diabetes results from the body's inability to produce or use insulin, which allows glucose (sugar) to accumulate in the BLOOD and spill over into the urine. Insulin therapy became the breakthrough in treatment that restored the potential for relatively normal lives for those who developed diabetes.

Type 1 Diabetes

Type 1 diabetes is an autoimmune disorder in which the IMMUNE SYSTEM produces antibodies that attack and destroy the cells of the islets of Langerhans. As a result, the body cannot produce insulin. An interplay between genetic and environmental factors is likely, with some researchers suspecting the autoimmune reaction follows INFECTION with a VIRUS. People who have type 1 diabetes must take regular insulin injections to meet their insulin needs and check their blood glucose levels

frequently to maintain as tight of a balance as possible between insulin and glucose. Type 1 diabetes most often develops before the age of 20, giving rise to its former designation as juvenile diabetes. Onset is usually rapid and pronounced. Type 1 diabetes requires lifelong insulin therapy.

Before current treatments many people who developed type 1 diabetes died from the condition or its complications before living much longer than early adulthood, making this a disease of the young. However, treatment approaches are significantly improved and many people who have type 1 diabetes now live well into old age with careful medical and lifestyle management. Some people refer to type 1 diabetes as insulin-dependent diabetes, which is no more accurate than the term juvenile diabetes because about 40 percent of people who have type 2 diabetes also require insulin therapy.

People who have type 1 diabetes have a higher likelihood of developing other AUTOIMMUNE DISORDERS of the endocrine system, notably thyroid conditions such as autoimmune THYROIDITIS and HYPOTHYROIDISM as well as autoimmune ADRENAL INSUFFICIENCY. Type 1 diabetes is also a component of complex endocrine disorders such as POLYGLANDULAR DEFICIENCY SYNDROME and MULTIPLE ENDOCRINE NEOPLASIA (MEN). Women who have well-controlled type 1 diabetes generally can conceive, carry, and deliver a PREGNANCY with few complications, though require close medical monitoring and diligent prenatal care. However, type 1 diabetes can affect FERTILITY in both women and men.

Type 2 Diabetes

Type 2 diabetes develops slowly, evolving over years and sometimes decades as a consequence of progressive INSULIN RESISTANCE. This form of diabetes most commonly develops in people who are age 50 or older, though can occur at any age (including childhood). A strong correlation exists between OBESITY and type 2 diabetes. Many health experts believe type 2 diabetes is fully preventable through lifestyle measures that incorporate nutritious EATING HABITS, daily physical exercise, and maintaining a healthy body weight. About 30 percent of people diagnosed with type 2 diabetes can control the condition through weight loss and lifestyle measures. The rest require oral antidia-

betes medications or insulin therapy. Type 2 diabetes may occur as a component of complex endocrine disorders, notably insulin resistance, as well as secondary to endocrine disorders affecting the adrenal cortex such as CUSHING'S SYNDROME (the adrenal steroid CORTISOL influences glucose METABOLISM).

Gestational Diabetes

Gestational diabetes develops during pregnancy as a consequence of the demands pregnancy places on the mother's body. A pregnant woman requires up to three times as much insulin to meet the needs of her body and the growing FETUS. However, the hormones that support pregnancy increase insulin resistance, reducing the woman's ability to use the insulin her body produces. The consequence may be temporary type 2 diabetes. Gestational diabetes affects about 4 percent of pregnant women in the United States. Some women can maintain appropriate insulin and glucose levels through careful nutritional habits, daily exercise, and WEIGHT LOSS AND WEIGHT MANAGEMENT. Others may require insulin therapy (many oral antidiabetes medications are not approved for use during pregnancy) for the duration of pregnancy.

Untreated gestational diabetes can have serious consequences for the baby, as the high levels of insulin in the mother's blood circulation increase the amount of glucose the baby's body can accept. One consequence is an unusually large baby. Rapid fetal growth is one indication that a woman might have gestational diabetes. About 70 percent of women who develop gestational diabetes recover completely. The rest develop permanent type 2 diabetes, either continuing after the end of the pregnancy or years to decades later.

Symptoms and Diagnostic Path

The symptoms of diabetes are similar across the types, though in type 1 may be rapid and severe. These symptoms include

- excessive thirst and frequent urination
- unexplained weight loss
- increased APPETITE
- changes in vision
- tingling in the hands and feet

- tiredness and weakness
- wounds or sores that heal slowly, or frequent infections (notably CANDIDIASIS)

The diagnostic path begins with a fasting blood glucose test, which measures the amount of glucose in the blood circulation after 12 hours without food or beverages other than water. Two separate results with blood glucose levels of 126 milligrams per deciliter of blood (126 mg/dL) confirm the diagnosis. Another blood test is glycosylated hemoglobin (HbA_{1c}), which measures a protein that indicates the stability of blood glucose levels over time. Normal HbA_{1c} is 4 to 6 percent; HbA_{1c} greater than 8 percent supports the diagnosis of diabetes. The doctor may choose to conduct a glucose-tolerance test, which measures the body's ability to respond to a rapid influx of glucose.

Treatment Options and Outlook

Treatment depends on the form of diabetes. Type 1 diabetes requires lifelong insulin therapy. About a third of people who have type 2 diabetes can manage the condition through weight loss and lifestyle measures (nutritious eating habits, daily exercise, and weight management), while the remainder require oral antidiabetes medications or insulin therapy. Ultimately about 40 percent of people who have type 2 diabetes will require insulin therapy, however, the underlying insulin resistance tends to be progressive within the dis-

ease process as well as with advancing age. Women who have gestational diabetes may be able to control the condition through lifestyle measures or may require treatment with oral antidiabetes medications approved for use in pregnancy or insulin therapy for the duration of the pregnancy.

Insulin therapy Therapeutic insulin is an injectable solution self-administered through subcutaneous injection (shots) one to several times a day. Until the 1990s most insulin products were the purified extracts culled from porcine (pig) and bovine (cow) pancreases. The biochemical structures of these extracts were close enough to human insulin to work in the human body, though in some people the differences were significant enough to activate an IMMUNE RESPONSE. In the 1990s laboratories began using RECOMBINANT DNA technologies to create synthetic insulin products biochemically and immunologically identical to endogenous human insulin. These insulins now allow precise dosaging and predictable actions within the body. Insulin doses are uniquely individual and may also vary with the person's activity level and other health conditions such as infections that cause FEVER. People taking insulin therapy check their blood glucose levels on a regular basis (one to several times daily) using a glucometer, which requires a fingerprick sample of blood.

Oral antidiabetes medications In 1958 the first oral medication to treat type 2 diabetes, the new

INSULIN PRODUCTS

Type of Action	Insulin Products	Onset	Peak Activity	Duration
rapid	lispro (Humalog)	5 to 15 minutes	45 to 90 minutes	3 to 4 hours
	aspart (NovoLog)	10 to 20 minutes	1 to 3 hours	3 to 5 hours
short	regular (R)	30 minutes	2 to 5 hours	5 to 8 hours
intermediate	neutral protamine	1 to 3 hours	6 to 12 hours	16 to 24 hours
	hagedorn (NPH) +	30 minutes	7 to 12 hours	16 to 24 hours
	lente (L) premixed (R + NPH)			
long	ultralente	4 to 6 hours	8 to 20 hours	24 to 28 hours
very long	glargine (Lantus)	1 hour	evenly over 24 hours	24 hours

sulfonylurea DRUG chlorpropamide (Diabinese), received approval for use in the United States. Sulfonylurea stimulates the beta islet cells to increase insulin production, raising the level of circulating insulin the blood. Subsequent generations of sulfonylureas have become more potent, more predictable, and less likely to cause side effects and are the foundation for oral therapy for type 2 diabetes. New sulfonylureas as well as new kinds of drugs to improve insulin sensitivity and influence glucose metabolism became available in the 1980s and 1990s. Many people who require treatment beyond lifestyle measures for type 2 diabetes take combinations of antidiabetes medications for optimal individualized control.

ORAL ANTIDIABETES MEDICATIONS	
Sulfonylureas	
acetohexamide (Dymelor)	chlorpropamide (Diabinese)
glimepiride (Amaryl)	glipizide (Glucotrol,
glyburide (DiaBeta)	Glucotrol XL)
tolazamide (Tolinase)	glyburide (Glynase PresTab,
tolbutamide (Orinase)	Micronase)
Biguanides	
metformin (Glucophage, Glucophage XR)	
Alpha-glucosidase inhibitors	
miglitol (Glyset)acarbose (Precose)	
Thiazolidinediones	
pioglitazone (Actos)rosiglitazone (Avandia)	
Meglitinides	
repaglinide (Prandin)	
d-Phenylalanine derivatives	
nateglinide (Starlix)	
Combination products	
glyburide + metformin (Glucovance)	

Lifestyle measures Nutritious eating habits, daily physical exercise, and healthy weight are critical factors especially in type 2 diabetes. Physical exercise improves the sensitivity of cells to insulin, allowing the body to become more efficient with insulin production. Most people who have diabetes do not require special diets though must monitor their consumption of food types to remain in balance with their medications (oral or insulin). Health-care providers recommend that all people diagnosed with diabetes and their fam-

ily members attend diabetes education workshops and classes available through hospitals and health-care clinics.

Risk Factors and Preventive Measures

Type 1 diabetes is not preventable, and likely results from an interaction of genetic and environmental factors that remain for researchers to identify. Type 2 diabetes, however, may be fully preventable through lifestyle choices that support healthy weight, nutritious eating habits, and daily physical activity. Long-term elevation of glucose in the blood causes extensive damage to the blood vessels and nerves. Complications of diabetes can be significant, though careful management of the diabetes can mitigate most of them. People who have any form of diabetes have increased risk for:

- CORONARY ARTERY DISEASE (CAD)
- HYPERTENSION (high BLOOD PRESSURE)
- RETINOPATHY of diabetes (damage to the RETINA)
- peripheral neuropathy (damage to the nerves)
- delayed wound HEALING and frequent infections, particularly a risk with the feet
- kidney disease and renal failure
- ERECTILE DYSFUNCTION in men and INFERTILITY in men and women

Most people who have diabetes are able to enjoy regular activities with appropriate treatment and lifestyle management.

See also ANTIBODY; DIABETES AND CARDIOVASCULAR DISEASE; DIABETES PREVENTION; HEALTH RISK FACTORS.

diabetes insipidus A condition of inadequate ANTIDIURETIC HORMONE (ADH) production or response. In health the HYPOTHALAMUS produces and the posterior lobe of the PITUITARY GLAND stores ADH. ADH acts on the KIDNEYS to regulate the amount of water they excrete into the URINE. The pituitary gland releases ADH when fluid levels in the body drop, causing the kidneys to withhold more water in the BLOOD. Diabetes insipidus can result from dysfunction of either the hypothalamus or the pituitary gland or disruption of communication between the two endocrine structures (central diabetes insipidus, or CDI), or as a conse-

quence of kidney disease (nephrogenic diabetes insipidus, or NDI).

A DIFFERENT DIABETES

Diabetes insipidus has no relationship to the familiar and common form of DIABETES, known clinically as diabetes mellitus, which is a dysfunction of INSULIN. Diabetes insipidus is a dysfunction of ANTIDIURETIC HORMONE (ADH). To avoid confusion, doctors commonly refer to diabetes insipidus as CDI (central diabetes insipidus) or NDI (nephrogenic diabetes insipidus).

Central Diabetes Insipidus (CDI)

CDI may result from lesions (growths) that affect the function of the hypothalamus, though more commonly as a result of trauma to the region of the BRAIN where the hypothalamus and pituitary gland are located. Such trauma may as a consequence of accidental injury (TRAUMATIC BRAIN INJURY), STROKE, or surgery. The hypothalamus may release inadequate amounts of ADH or the pituitary gland may fail to respond. CDI may also occur when an ADENOMA (noncancerous tumor) grows in the posterior lobe of the pituitary gland and inhibits ADH secretion.

Nephrogenic Diabetes Insipidus (NDI)

In severe kidney disease or RENAL FAILURE the kidneys themselves do not respond to ADH. This leaves the kidneys unable to concentrate the urine. They consequently pass into the urine as much water as passes through them in the blood. Medications that interfere with kidney function may cause NDI. Lithium, taken to treat BIPOLAR DISORDER, and the ANTIBIOTIC MEDICATIONS demeclocycline and amphotericin B, are the most common culprits when NDI is DRUG induced.

Symptoms and Diagnostic Path

Whether central or nephrogenic, diabetes insipidus symptoms are the same. They are

- extreme thirst (called polydipsia) and often a craving for ice water
- frequent urination (called polyuria), including through the night (NOCTURIA)

It is not uncommon for a person who has diabetes insipidus to drink and urinate up to 20 liters

or more every 24 hours. When symptoms develop gradually and water intake keeps pace with urination, the person may not experience the symptoms as unusual events. Diabetes insipidus results in health complications (such as electrolyte imbalance) only when the person is unable to match fluid input and output. The diagnostic path is primarily clinical (based on symptoms) with a water deprivation test to confirm the diagnosis. For this test, the person remains under continuous medical observation while consuming no water. Hourly urine tests measure the concentration of the urine. In a healthy person the urine becomes increasingly concentrated with restricted fluid consumption. In diabetes insipidus the urine remains dilute.

Because excessive thirst and urination are also symptoms of diabetes mellitus, the endocrinologist is likely to conduct blood tests to measure blood GLUCOSE and INSULIN levels. The endocrinologist may also choose to conduct diagnostic imaging procedures such as MAGNETIC RESONANCE IMAGING (MRI) or COMPUTED TOMOGRAPHY (CT) SCAN to identify traumatic injury or tumors in CDI.

Treatment Options and Outlook

Treatment targets any identified underlying cause. Thiazide diuretic medications, which ordinarily increase urination, have the opposite effect in both CDI and NDI because of their actions on the kidneys. HORMONE THERAPY with medications such as desmopressin or lyspressin nasal spray is usually effective for CDI. Even when the person is able to maintain fluid balance, it is important to treat diabetes insipidus because the untreated condition results in kidney damage over time. Treatment minimizes or eliminates symptoms for most people.

Risk Factors and Preventive Measures

The primary risk factor for CDI is head trauma, in which case early intervention and treatment are most effective. Chronic kidney disorders such as POLYCYSTIC KIDNEY DISEASE are commonly the cause of NDI. Appropriately treating these disorders mitigates the NDI. It is important for people who have CDI or NDI to drink enough water to remain hydrated, to prevent complications arising from electrolyte imbalance.

See also [HYPERCALCEMIA](#); [HYPOKALEMIA](#); [HYPONATREMIA](#); [LESION](#); [SARCOIDOSIS](#); [SICKLE CELL DISEASE](#).

dopamine A peptide the adrenal medulla of the ADRENAL GLANDS, the HYPOTHALAMUS, and other structures in the BRAIN produce. Dopamine functions in the body as a HORMONE, when synthesized by the adrenal medulla, and as a NEUROTRANSMITTER when synthesized by brain structures or NERVE cells. NOREPINEPHRINE is a dopamine precursor (substance the body uses as the basis for dopamine synthesis).

Hormonal dopamine, also called PROLACTIN release-inhibiting factor (PRIF), is an inhibitory hormone that acts to prevent the release of the pituitary hormone prolactin. Dopamine also has less pronounced inhibitory action for FOLLICLE-STIMULATING HORMONE (FSH), LUTEINIZING HORMONE (LH), and THYROID-STIMULATING HORMONE (TSH). The hypothalamus directs the adrenal medulla to release dopamine through the neurotransmitter acetylcholine. As a neurotransmitter, dopamine is critical to voluntary MUSCLE control and move-

ment, cognitive function, mood, emotion, and perceptions of pleasure. Dopamine appears to play a key role in ADDICTION such as to NARCOTICS and NICOTINE (cigarette smoking).

Dopamine is also a pharmaceutical DRUG used to treat CARDIAC ARREST and cardiovascular SHOCK. When injected intravenously to establish dopamine levels higher than normal in the bloodstream, dopamine constricts (narrows) peripheral BLOOD vessels to direct more blood to critical organs, intensifies the force of the HEART'S contractions to increase the amount of blood the heart pumps, and increases the HEART RATE. The dopamine precursor levodopa is a treatment for PARKINSON'S DISEASE (a degenerative neurologic disorder that results from inadequate dopamine production in the sections of the brain that control movement).

For further discussion of dopamine within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also [EPINEPHRINE](#).

endocrine gland A structure, sometimes called a ductless gland, within the body that produces chemicals, called hormones, it secretes directly into the bloodstream. Hormones influence the function of cells that contain receptors for them. The **PITUITARY GLAND**, **ADRENAL GLANDS**, and **THYROID GLAND** are examples of endocrine glands. An exocrine gland, by contrast, secretes the chemicals it produces into ducts (specialized channels) for release into body structures. The **SALIVARY GLANDS** and **SWEAT GLANDS** are examples of exocrine glands. The **KIDNEYS**, gastrointestinal tract, and **PLACENTA** in a pregnant woman also contain endocrine structures.

Three mechanisms can trigger endocrine activity. They are

- humoral, in which the endocrine system responds to chemicals in the bloodstream such as calcium (triggering **CALCITONIN** release from the thyroid gland or **PARATHYROID HORMONE** from the **PARATHYROID GLANDS**)
- hormonal, in which the hormones from one endocrine gland direct activity from other endocrine glands such as the **STRESS RESPONSE HORMONAL CASCADE**
- neurologic, in which **NERVE** impulses stimulate endocrine action such as from the **HYPOTHALAMUS** to the posterior lobe of the pituitary gland

Sometimes the neurologic system and the endocrine system secrete the same chemicals, such as **EPINEPHRINE** and **NOREPINEPHRINE**. When endocrine structures synthesize these chemicals, they are hormones and they travel to their target cells through the blood circulation. When the neurologic system synthesizes these structures, they are neurotransmitters, and they travel to

their target cells through interstitial fluid (fluid between cells). Neurotransmitters travel to their destinations, elicit reactions, and dissipate more rapidly than hormones.

THE ENDOCRINE GLANDS

ADRENAL GLANDS	HYPOTHALAMUS	ISLETS OF LANGERHANS
OVARIES	PARATHYROID GLANDS	PINEAL GLAND
PITUITARY GLAND	PLACENTA	TESTES
THYMUS	THYROID GLAND	

For further discussion of the endocrine glands within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also [DIGESTIVE HORMONES](#); [NEUROTRANSMITTER](#).

epinephrine A chemical the adrenal medulla of the **ADRENAL GLANDS** and the synaptic vesicles of the **NERVE** endings produce. Epinephrine, also called adrenaline, functions in the body as a peptide **HORMONE** when synthesized by the adrenal medulla and as a **NEUROTRANSMITTER** when synthesized in the **BRAIN** or nerve endings. Among the hormones activated in the **STRESS RESPONSE HORMONAL CASCADE**, epinephrine

- constricts peripheral **BLOOD** vessels to centralize blood flow and raise **BLOOD PRESSURE**
- dilates bronchial structures in the **LUNGS** to increase air flow
- initiates rapid conversion of glycogen to **GLUCOSE** in the **LIVER** to raise the blood glucose level and increase energy to the cells
- intensifies the **HEART'S** contractions to increase **CARDIAC OUTPUT** (the amount of blood the heart pumps out with each **CARDIAC CYCLE**)
- accelerates the **HEART RATE**

In the brain, epinephrine is an active and abundant neurotransmitter in numerous neurologic functions, including heightened alertness and cognitive function during stressful situations. Epinephrine is also a pharmaceutical DRUG used to treat CARDIAC ARREST and cardiovascular SHOCK. When injected intravenously to produce blood levels significantly higher than normal in the bloodstream, epinephrine causes accelerated actions such as those it initiates as an endogenous hormone in the stress response. It also stabilizes the electrical activity of the heart to normalize the heart's rhythm (antiarrhythmic). In other pharmaceutical applications epinephrine blocks the body's inflammatory response in severe allergic reactions and anaphylactic shock, and can reduce bleeding and extend the effectiveness of injected local anesthetics.

EPINEPHRINE, ADRENALINE, OR ADRENALIN?

Epinephrine, adrenaline, and Adrenalin are the same chemical. Adrenalin (no e) is a proprietary DRUG trademarked in the United States. Epinephrine and adrenaline designate either the endogenous chemical (HORMONE or NEUROTRANSMITTER) or the GENERIC DRUG. Only the United States uses the term *epinephrine*. Other countries follow the international standard terminology, which uses the term *adrenaline*. This is because in the United States trademark protections prevent alternate names for trademarked products that could be confused with the trademark.

For further discussion of epinephrine within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also [DOPAMINE](#); [NOREPINEPHRINE](#).

estrogens A collective term for the "female" sex hormones, including prohormones (chemical precursors the body converts to hormones) and metabolites (byproducts of HORMONE METABOLISM). Estrogens are among the steroid hormones the body synthesizes from cholesterol. Estrogens derive from ANDROGENS (the "male" sex hormones).

Common use applies the singular term estrogen to refer to any or all of the three endogenous (naturally occurring within the body) estrogen hor-

mones: estradiol, estriol, and estrone. Estradiol is the most potent and most biochemically active of the estrogens. Estrone is very similar in chemical structure to estradiol though exerts a weaker response. Estriol is a metabolite of both estradiol and estrone.

In a woman's body the levels of these closely related hormones change at MENARCHE and at MENOPAUSE, and fluctuate within the menstrual cycle and with PREGNANCY. Estradiol is the predominant estrogen during the years of FERTILITY, with the less-potent estrone moving into dominance after menopause. In a man's body estrogen levels remain fairly constant. The HYPOTHALAMUS's secretion of GONADOTROPIN-RELEASING HORMONE (GNRH) regulates the hormonal cascade for production and release of the estrogens. In women this cascade is cyclic, establishing the monthly menstrual cycle during the four decades or so a woman is fertile.

Men and women alike have estrogens (just as both sexes also have androgens). The OVARIES in women, the TESTES in men, and the adrenal cortex of the ADRENAL GLANDS in men and women synthesize (produce) most of the estrogens in the BLOOD circulation. During pregnancy the PLACENTA produces estrogens as well. Adipose (fat) cells and the LIVER in both sexes, and the breasts in women, also synthesize small amounts of estrogens.

In women the estrogens establish secondary sex characteristics and fertility, and maintain pregnancy. The estrogens are essential in both sexes for cholesterol metabolism, BONE calcium content and density, thyroid function, SKIN health, and collagen maintenance. The estrogens also have roles in mood and emotion, probably in both men and women though more pronounced in women because estrogen levels fluctuate with the menstrual cycle.

Various endocrine disorders may result in estrogen levels that are too high or too low, with consequences for fertility in women and for cholesterol metabolism in men and women. Doctors use pharmaceutical preparations of estrogens and estrogen analogs (drugs that bind with estrogen receptors though do not have estrogen activity) for a diverse array of therapeutic applications including CONTRACEPTION (birth control pills), treatment for HORMONE-DRIVEN CANCERS (notably PROSTATE

CANCER) in men, OSTEOPOROSIS and BREAST CANCER prevention in women (estrogen analogs), and fertility treatments in women.

Estrogen products were a mainstay of therapy (alone or in combination with PROGESTERONE) to relieve the discomforts of menopause for much of the latter half of the 20th century. Research in the early 2000s demonstrated significant risks with routine hormone replacement therapy (HRT), however, resulting in a change in medical practice to use such products within narrow therapeutic guidelines and for the shortest amount of time possible to achieve a therapeutic result.

For further discussion of estrogen within the context of the endocrine system’s structure and function please see the overview section “The Endocrine System.”

See also CHLOASMA; ENDOMETRIAL CANCER; FOLLICLE-STIMULATING HORMONE (FSH); GYNECOMASTIA; HORMONE THERAPY; HYPOGONADISM; HYPOTHYROIDISM; INFERTILITY; LUTEINIZING HORMONE (LH); MENSTRUATION; PHYTOESTROGENS; POLYCYSTIC OVARY SYNDROME (PCOS); TESTOSTERONE; THYROID GLAND.

euthyroid sick syndrome A circumstance in which BLOOD tests show irregular thyroid HORMONE levels in the blood but hypothalamic, pituitary, and thyroid functions are all normal. Euthyroid sick syndrome typically accompanies a severe acute illness or chronic condition. Many medications interfere with thyroid function, altering thyroid hormone levels in the blood. Because the body experiences significant physiologic stress with severe illness, many of the body’s natural hormonal responses have the consequence of altering thyroid hormone levels.

Typically there are no symptoms of hypothyroidism with euthyroid sick syndrome, though the symptoms of the health condition may make this difficult to assess. Declining thyroid hormone levels, measured through blood tests, provide important insight into the overall crisis state the body is experiencing. There appears to be no benefit in treating euthyroid sick syndrome with replacement thyroid hormones, so most doctors choose a course of watchful waiting in regard to thyroid function and focus therapeutic efforts on the causative condition. Thyroid hormone levels gradually return to normal as the person recovers from

the underlying acute illness or when the chronic condition improves.

CONDITIONS THAT MAY RESULT IN EUTHYROID SICK SYNDROME	
BONE MARROW TRANSPLANTATION	BURNS
CANCER	CARDIOMYOPATHY
chronic CIRRHOSIS	CHRONIC OBSTRUCTIVE
DIABETES	PULMONARY DISEASE (COPD)
GLOMERULOSCLEROSIS	GLOMERULONEPHRITIS
INFLAMMATORY BOWEL DISEASE (IBD)	HEART FAILURE
ISCHEMIC HEART DISEASE (IHD)	major surgery
MYOCARDIAL INFARCTION	ORGAN TRANSPLANTATION
PANCREATITIS	POLYGLANDULAR DEFICIENCY
RENAL FAILURE	SYNDROME
SARCOIDOSIS	severe GASTROENTERITIS
SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)	major trauma

See also GOITER; HYPERTHYROIDISM; THYROID GLAND.

follicle-stimulating hormone (FSH) A peptide HORMONE the anterior lobe of the PITUITARY GLAND secretes in response to stimulation from the HYPOTHALAMUS’s release of GONADOTROPIN-STIMULATING HORMONE (GNHR). In women, FSH stimulates the follicles in the OVARIES to bring eggs (OVA) to maturity. In men, FSH stimulates growth of cells in the TESTES and synthesis of proteins necessary to support spermatogenesis (production of SPERM). The actions of FSH closely intertwine with those of another pituitary hormone, LUTEINIZING HORMONE (LH). Pituitary tumors can interfere with FSH synthesis, causing the pituitary gland to produce inadequate or excessive amounts. Extended use of ANABOLIC STEROIDS AND STEROID PRECURSORS suppresses both GnRH and FSH (as well as LH), resulting in symptoms of HYPOGONADISM that are most pronounced in men though can occur in women as well. HORMONE THERAPY as treatment for PROSTATE CANCER has the same effect.

For further discussion of FSH within the context of the endocrine system’s structure and function please see the overview section “The Endocrine System.”

See also ANDROGENS; ANTIDIURETIC HORMONE (ADH); CRYPTORCHIDISM; ESTROGENS; FERTILITY; GROWTH HORMONE (GH); KLINEFELTER’S SYNDROME; INFERTILITY; OXYTOCIN; PROLACTIN; THYROID-STIMULATING HORMONE (TSH); TURNER’S SYNDROME.



gastric inhibitive polypeptide (GPI) See DIGESTIVE HORMONES.

gastrin See DIGESTIVE HORMONES.

glucagon A peptide HORMONE the alpha cells of the ISLETS OF LANGERHANS produce in response to low blood GLUCOSE levels (humoral regulation). Intense physical exercise also causes the release of glucagon into the bloodstream. Glucagon stimulates the LIVER to convert glycogen (a storage form of glucose) into glucose to raise the level of glucose in the BLOOD. Glucagon opposes the action of INSULIN (which stimulates glucose use or conversion to glycogen to decrease blood glucose levels). High blood glucose levels inhibit glucagon production as does release of SOMATOSTATIN, another peptide hormone synthesized by the HYPOTHALAMUS, gastrointestinal tract, and delta cells of the islets of Langerhans. Glucagon is also available as a pharmaceutical DRUG used to treat HYPOGLYCEMIA (low blood glucose) and insulin shock.

For further discussion of glucagon within the context of the endocrine system’s structure and function please see the overview section “The Endocrine System.”

See also DIABETES; DIGESTIVE HORMONES; LIVER; METABOLISM.

glucose A simple sugar molecule (monosaccharide) that is the primary energy source for most cells in the body. The body metabolizes (breaks down) carbohydrates, which enter the body from the gastrointestinal tract, into glucose. The body requires a fairly narrow but constant level of available glucose circulating in the BLOOD at all times (70 to 110 milligrams of glucose per deciliter of blood). Glucose and two hormones the ISLETS OF

LANGERHANS in the PANCREAS produce, INSULIN and GLUCAGON, function in synchronization and opposition to maintain this level.

Rising glucose levels in the blood signal the islets of Langerhans to secrete insulin. The insulin binds with receptors on cell membranes, enabling glucose to enter the cells. Within the cell the glucose causes a series of biochemical actions that result in the formation of adenosine triphosphate (ATP), which fuels cellular METABOLISM. Insulin (in coordination with CORTISOL) also stimulates the LIVER to extract excess glucose from the blood and convert it to glycogen, a storage form of glucose the liver then deposits within its tissues as well as within MUSCLE tissue throughout the body. When the blood glucose level drops, the islets of Langerhans release glucagon, a hormone that causes the liver to convert glycogen back to glucose and release it into the blood circulation. Glucagon also stimulates DIGESTIVE HORMONES and enzymes that result in the sensation of hunger, encouraging food intake that can more rapidly replenish the body’s glucose supply.

FASTING BLOOD GLUCOSE LEVELS	
Health Condition	Milligrams of Glucose per Deciliter of Blood
hypoglycemia	< 50
normal	70–110
hyperglycemia (prediabetes)	111–125
DIABETES	> 126

See also CELL STRUCTURE AND FUNCTION.

goiter Swelling and enlargement of the THYROID GLAND. Most often goiter occurs as a symptom of thyroid dysfunction though can develop when thyroid function is normal, such as sometimes

occurs as a consequence of PREGNANCY (when the body's need for thyroid hormones increases) or in EUTHYROID SICK SYNDROME (when a health crisis disrupts the entire endocrine matrix). A goiter may cause uniform enlargement of the thyroid gland (diffuse goiter) or isolated enlargement (nodular goiter). Though typically a goiter is visible on the front of the neck, occasionally a nodular goiter forms on the back of a thyroid lobe, near the end, pressuring the airway. Among the numerous causes of goiter are

- iodine deficiency
- HYPOTHYROIDISM (underactive thyroid)
- HYPERTHYROIDISM (overactive thyroid), including GRAVES'S DISEASE
- THYROIDITIS (INFLAMMATION of the thyroid gland)
- radiation exposure (such as from RADIATION THERAPY to treat CANCER of the larynx, MOUTH, or upper chest)
- thyroid nodules (noncancerous growths)
- THYROID CANCER

Hypothyroidism, hyperthyroidism, and thyroiditis are the most common causes of diffuse goiter. Thyroid nodules, which are fairly common, and thyroid cancer, which is relatively uncommon, are more likely to cause nodular goiter. Iodine deficiency is rare in the United States because most table salt is iodized. Symptoms of goiter may include

- visible swelling on one side or both sides of the neck
- palpable lump in the neck, especially when swallowing
- difficulty swallowing or the sensation of something being stuck in the THROAT
- difficulty breathing, usually with exhalation

Many people also have symptoms of hypothyroidism or hyperthyroidism, when either condition is the cause of the goiter. The diagnostic path includes blood tests to measure the level of thyroid hormones, ULTRASOUND of the neck, and often a radionuclide scan or COMPUTED TOMOGRAPHY (CT) SCAN. Treatment depends on the findings and the extent to which symptoms interfere with func-

tions such as swallowing or BREATHING. If surgery to remove the thyroid gland is necessary (thyroidectomy), the person will need to take lifelong thyroid supplementation (thyroid HORMONE THERAPY). Endocrinologists typically take an approach of watchful waiting with a goiter that causes no symptoms and does not affect thyroid function (thyroid hormone levels are normal).

See also AUTOIMMUNE DISORDERS; LYMPHOMA; THYROID NODULE.

gonadotropin-releasing hormone (GnRH) A peptide HORMONE, also called luteinizing hormone-releasing hormone (LHRH), the HYPOTHALAMUS produces to stimulate the anterior lobe of the PITUITARY GLAND to synthesize and release LUTEINIZING HORMONE (LH) and FOLLICLE-STIMULATING HORMONE (FSH). LH and FSH in turn stimulate the gonads, or sex glands, to produce their respective hormones. In women the effect stimulates the OVARIES to produce ESTROGENS and PROGESTERONE, and in men stimulates the TESTES in men to produce TESTOSTERONE. When these sex hormones reach certain levels in the bloodstream the hypothalamus stops secreting GnRH, and the gonadotropic cascade stops—a negative-feedback loop. In women these levels fluctuate according to the menstrual cycle. Other hormones may also influence the release of GnRH.

Doctors sometimes use a pharmaceutical preparation of GnRH, called a GnRH analog, to treat ENDOMETRIOSIS. Because its chemical composition is nearly identical to that of endogenous GnRH, a GnRH analog binds with GnRH receptors to block endogenous GnRH binding. This prevents the release of LH and FSH, and consequently suppresses the menstrual cycle and OVULATION.

For further discussion of GnRH within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ANTIDIURETIC HORMONE (ADH); GROWTH HORMONE (GH); INHIBIN; MENSTRUATION; OXYTOCIN; PROLACTIN; THYROID-STIMULATING HORMONE (THS).

Graves's disease An autoimmune disorder in which the body produces antibodies that attack the THYROID GLAND, producing symptoms of HYPERTHYROIDISM (overactive thyroid gland). The most

common cause of hyperthyroidism, Graves's disease affects seven times as many women as men and is most frequent among women between the ages of 30 and 60. Graves's disease is more likely to occur among people who have other AUTOIMMUNE DISORDERS, notably type 1 DIABETES, SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), and POLYGLANDULAR DEFICIENCY SYNDROME.

In health the HYPOTHALAMUS, PITUITARY GLAND, and thyroid gland work in synchronization to maintain an appropriate balance of thyroid hormones, which regulate METABOLISM, in the BLOOD circulation. Low blood levels of the major thyroid hormones TRIIODOTHYRONINE (T_3) and THYROXINE (T_4) signal the hypothalamus to produce THYROTROPIN-RELEASING HORMONE (TRH). TRH in turn stimulates the pituitary gland to secrete THYROID-STIMULATING HORMONE (TSH). TSH binds with TSH receptors on the cells of the thyroid gland, activating synthesis of T_3 and T_4 . When T_3 and T_4 reach appropriate levels in the bloodstream, the hypothalamus stops producing TRH and the thyroid hormone cascade ends.

The antibodies the IMMUNE SYSTEM produces in Graves's disease, called thyroid-stimulating immunoglobulins (TSIs), continuously stimulate the TSH receptors in the thyroid gland, falsely signaling that blood T_3 and T_4 levels are too low. The thyroid gland responds by increasing synthesis of these hormones. It is an overproduction, however. TSH and TRH levels fall as they should but thyroid hormone production continues in the thyroid gland, resulting in hyperthyroidism. Graves's disease accounts for about 70 percent of hyperthyroidism in the United States.

A serious corollary condition is GRAVES'S OPTHALMOPATHY, in which the excessive thyroid hormones cause swelling in and around the structures of the eyes. Graves's ophthalmopathy is often the earliest indication of Graves's disease and can result in permanent damage to the eyes, including loss of vision. The characteristic symptom of Graves's ophthalmopathy is EXOPHTHALMOS (bulging eyes, also called poptosis). Some endocrinologists believe Graves's ophthalmopathy is a distinct autoimmune disease process separate from Graves's disease, as it may exist without apparent hyperthyroidism or develop years to decades before or after hyperthyroidism manifests.

Symptoms and Diagnostic Path

The symptoms of Graves's disease are those of hyperthyroidism and may include symptoms of Graves's ophthalmopathy as well. These symptoms are

- PALPITATIONS
- weight loss
- heat intolerance
- difficulty concentrating
- irritability, anxiety, and insomnia (difficulty sleeping)
- bulging eyes (poptosis), "lid lag" (delay in the eyelid's movement when the EYE moves downward), and vision disturbances (Graves's ophthalmopathy)

The diagnostic path includes blood tests to measure thyroid hormones (typically T_3 , T_4 , and TSH) and the presence of TSIs. The former establish hyperthyroidism; the latter confirms the diagnosis of Graves's disease.

Treatment Options and Outlook

Treatment targets disabling the thyroid gland's ability to synthesize thyroid hormones. Because Graves's disease is a progressive autoimmune disorder, endocrinologists tend to opt for permanent therapies such as radioactive iodine (^{131}I) to destroy thyroid tissue so it cannot produce thyroid hormones. One consequence of this approach is that the destruction of the thyroid gland results in permanent hypothyroidism and makes necessary lifelong HORMONE THERAPY with thyroid hormone supplements. Thyrotoxic medications such as methimazole and propylthiouracil (PTU), though effective in other forms of hyperthyroidism, are less successful because the autoimmune response continues.

Risk Factors and Preventive Measures

Women who have other autoimmune disorders have increased risk for Graves's disease. For them, regular blood tests to measure thyroid hormones can help detect the condition early. Routine ophthalmologic examinations can detect Graves's ophthalmopathy, which may develop even with treatment for Graves's disease, before it causes

permanent damage to the eyes and vision. No known preventive measures exist for Graves's disease.

See also IMMUNE RESPONSE; LYMPHOCYTE; **THYROIDITIS**; **THYROID STORM**; VISION HEALTH.

growth hormone (GH) A peptide HORMONE the PITUITARY GLAND produces in response to secretion of GROWTH HORMONE–RELEASING HORMONE (GHRH) by the HYPOTHALAMUS. GH affects growth directly by initiating an increase in cell division and indirectly by stimulating the production of insulinlike growth factors (IGFs), proteins that affect cell METABOLISM and other functions. GH levels are highest in childhood, then taper off in early adulthood to maintain a stable level. GH remains essential in adulthood to maintain appropriate cell metabolism, notably in BRAIN, MUSCLE, and fat cells. GROWTH HORMONE DEFICIENCY in childhood results in stunted growth, and in adulthood can result in diminished cognitive function, decreased muscle mass, and increased body fat. Some researchers believe the decline in GH in adulthood contributes to the aging process, though the mechanisms through which this occurs remain unknown. Excessive GH secretion, such as may occur with a pituitary ADENOMA, results in ACROMEGALY.

For further discussion of growth hormone within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ADRENOCORTICOTROPIN HORMONE (ACTH); ANABOLIC STEROIDS AND STEROID PRECURSORS; ANTIDIURETIC HORMONE (ADH); FOLLICLE-STIMULATING HORMONE (FSH); HUMAN GROWTH HORMONE (HGH) SUPPLEMENT; LUTEINIZING HORMONE (LH); OXYTOCIN; PROLACTIN; THYROID-STIMULATING HORMONE (TSH).

growth hormone deficiency An endocrine disorder in which the anterior lobe of the PITUITARY GLAND produces an inadequate amount of GROWTH HORMONE (GH). GH is fundamental for proper growth and development in childhood and remains essential for appropriate metabolic function in adulthood. In childhood GH binds to receptors in BONE cells that increases the rate at which they divide, causing bone growth that results in increased height. In adulthood GH deficiency can affect cognitive functions and memory,

body mass and fat distribution, and numerous aspects of cell METABOLISM.

It is important to distinguish between abnormal growth and a child who is simply short in stature. The average rate of growth for children is about two inches a year. Many factors influence a child's ultimate height. Indications in addition to short stature that a child may have GH deficiency include accumulations of body fat in the abdomen and the face (giving a rounded, chubby appearance), delayed eruption of TEETH, and in an older child, delayed PUBERTY. The diagnostic path includes

- BLOOD tests to measure thyroid hormones (HYPOTHYROIDISM can cause slowed growth) and insulinlike growth factors (IGFs)
- measuring height and weight over a period of time to detect growth patterns
- X-rays and sometimes COMPUTED TOMOGRAPHY (CT) SCAN to evaluate bone structure
- a GROWTH HORMONE–RELEASING HORMONE (GHRH) challenge test to measure the ability of the pituitary gland to respond to stimulation by GHRH

Treatment for confirmed GH deficiency in children is injections of recombinant human growth hormone (hGH), a genetically engineered substance that has the precise configuration of endogenous GH, continued until the child reaches appropriate growth. Some people develop antibodies to the recombinant hGH, decreasing its effectiveness. When the pituitary gland is congenitally absent (a birth defect) or permanently damaged, long-term hGH therapy may be necessary. Whether treatment continues into adulthood depends on symptoms and the cause of the deficiency. Doctors do not agree on the definition or the need for treatment of adult growth hormone deficiency that does not begin in childhood.

See also ACROMEGALY; ADRENAL INSUFFICIENCY; HUMAN GROWTH HORMONE (HGH) SUPPLEMENT; POLYGLANDULAR DEFICIENCY SYNDROME; TURNER'S SYNDROME.

growth hormone–releasing hormone (GHRH) A peptide HORMONE the HYPOTHALAMUS produces to stimulate the PITUITARY GLAND to synthesize and

release GROWTH HORMONE (GH). The secretion of GHRH initiates a cascade of chemical activity that results in intensified cell METABOLISM and processes that promote cell division and the growth of body tissues and structures. The hormone SOMATOSTATIN, which the hypothalamus and the delta cells of the ISLETS OF LANGERHANS produce, provides the stimulus for the hypothalamus to stop releasing GHRH. Multiple factors regulate the balance between GHRH and somatostatin.

For further discussion of GHRH within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also [ACROMEGALY](#); ADRENOCORTICOTROPIN HORMONE (ACTH); ANABOLIC STEROIDS AND STEROID PRECURSORS; ANTIDIURETIC HORMONE (ADH); FOLLICLE-STIMULATING HORMONE (FSH); GROWTH HORMONE DEFICIENCY; LUTEINIZING HORMONE (LH); OXYTOCIN; PROLACTIN; THYROID-STIMULATING HORMONE (TSH).



Hashimoto's disease See THYROIDITIS.

hemochromatosis A genetic disorder in which the gastrointestinal tract absorbs too much iron into the bloodstream. The BLOOD deposits the excess iron in various tissues and organs, where it accumulates and eventually causes damage. Common sites for deposits include the HEART, causing HEART FAILURE, PANCREAS, causing DIABETES, and LIVER, causing CIRRHOSIS and LIVER FAILURE. Though hemochromatosis is congenital (present from birth), most people do not experience consequences or symptoms until midlife when enough iron has accumulated in the organs to affect their functions.

Health experts believe hemochromatosis is far more common than the number of people diagnosed with the condition suggests. Women may not show symptoms until 10 or more years after MENOPAUSE because the bleeding associated with MENSTRUATION reduces blood iron concentrations, serving as a natural therapy for the hemochromatosis. Researchers have identified several GENE mutations that can cause hemochromatosis. The most common mutations are those involving the HFE gene that regulates gastrointestinal iron absorption. Researchers have designated them C282Y and H63D, and they account for about 85 percent of diagnosed hemochromatosis in the United States.

Symptoms and Diagnostic Path

Doctors often detect hemochromatosis during evaluation for other health concerns, when blood tests show higher than normal HEMOGLOBIN or iron levels. The symptoms of hemochromatosis result from damage to organs and structures where iron deposits accumulate and often take the form of

fairly advanced disease states by the time of detection. General symptoms may include

- JOINT PAIN (the most common symptom)
- fatigue and lethargy
- abdominal discomfort or PAIN

The excessive iron in the body may also interfere with FERTILITY (causing early menopause in women) and LIBIDO (sex drive). The diagnostic path includes general blood tests to measure hemoglobin, hematocrit, red blood cells, and specialized blood tests that measure iron. The most commonly used are

- transferrin saturation, which measures how much iron the hemoglobin carries (protein saturation)
- total iron binding capacity (TIBC), which measures the capacity of the hemoglobin to transport iron
- serum ferritin, which measures the iron the liver contains

Elevated results in any of these tests suggests hemochromatosis. Further blood analysis to detect the HFE gene mutation and liver biopsy are the final steps in the diagnostic path and provide a definitive diagnosis.

Treatment Options and Outlook

Treatment for hemochromatosis is phlebotomy, the withdrawal of blood a pint at a time. Initial treatment may take place several times a week until blood levels of iron return to normal. Most people then require phlebotomy sessions only once every two to four months, though lifelong treatment is necessary. Treatment also targets any

health conditions that have developed as a consequence of iron deposits, such as heart disease or diabetes. The damage iron deposits cause is irreversible, though once treatment begins most secondary conditions improve.

DONATING BLOOD

Some BLOOD banks and blood collection centers accept blood withdrawn as treatment hemochromatosis for donation and use it to produce blood products. As blood products are limited and sometimes scarce, it is worthy for people who are receiving therapeutic phlebotomy for hemochromatosis to look for centers who will accept their blood for such use. Otherwise the center discards the blood.

Risk Factors and Preventive Measures

Because hemochromatosis is hereditary, the key risk for developing it is family history. Doctors have only recently recognized the potentially widespread existence of hemochromatosis, however; and many family medical histories make no reference to the condition. People who have family histories for early-onset liver disease, heart disease, or diabetes should have basic blood tests for iron levels included with their routine medical examinations as a screening precaution. Early diagnosis and treatment prevent most of the complications that can develop and minimize the severity of the condition and its affect on health.

See also BLOOD DONATION; PHENYLKETONURIA (PKU); WILSON'S DISEASE.

hirsutism Excessive growth of body HAIR in a male pattern, typically involving the face, chest, back, arms, and legs. The hair follicles on these SKIN surfaces are sensitive to TESTOSTERONE and other ANDROGENS ("male" hormones), the hormones that stimulate hair growth in both men and women. Though hirsutism affects men and women, it is especially a concern for women for clinical as well as cosmetic reasons. Hirsutism may result from the hair follicles being overly sensitive to the effects of androgens (with normal levels of androgens in the BLOOD) or an excess of androgens in the blood circulation.

In the latter circumstance, researchers believe the culprit is overactivity of an enzyme, 5-alpha

reductase, that converts testosterone to dihydrotestosterone, the androgen form that stimulates hair growth. Excessive blood levels of testosterone may result from androgen-secreting tumors that form in the OVARIES or the adrenal cortex of the ADRENAL GLANDS, the two primary sources of endogenous testosterone. Women athletes who use ANABOLIC STEROIDS AND STEROID PRECURSORS may also develop hirsutism. INSULIN RESISTANCE and POLYCYSTIC OVARY SYNDROME (PCOS), existing independently or as constituents of INSULIN resistance, are strongly associated with hirsutism in women. In some situations the endocrinologist cannot determine a definitive cause for hirsutism (idiopathic hirsutism).

The diagnostic path includes blood tests to measure hormone levels, hormonal responses, and insulin sensitivity. The precise tests depend on the findings of preliminary tests. ULTRASOUND OR MAGNETIC RESONANCE IMAGING (MRI) of the ovaries or imaging procedures to visualize the adrenal glands may identify any tumors. Treatment depends on any identified cause and may combine HORMONE THERAPY to suppress androgen production or binding with cosmetic therapies to remove or minimize excessive hair. The most commonly used hormone therapy is the oral contraceptive (birth control pill), which regulates the hormonal cycle of the ovaries. The endocrinologist may prescribe other hormone products, such as CORTICOSTEROID MEDICATIONS, to suppress the HORMONE production of the adrenal cortex. These methods are effective for many though not all people who have hirsutism. Cosmetic approaches include electrolysis or laser therapy to permanently destroy hair follicles. Shaving and chemical depilatories (hair removers) are sometimes effective though require frequent use. Hirsutism can be emotionally difficult for those who have it, especially women, though men as well may find the condition distressing.

See also CONTRACEPTION; GENETIC DISORDERS; PORPHYRIA.

hormone A chemical that travels through the blood circulation and influences the functions of cells within the body. The body produces dozens of hormones of two primary chemical forms, peptides and steroids. A hormone affects only the cells that have receptors for it, and only when it binds

to those receptors. A receptor is somewhat like an outlet that has a unique configuration. The hormone for which the receptor is sensitive matches that configuration, forming a chemical “lock” between the hormone molecule and the cell. Through such binding hormones cause chemical changes within the cell that may activate enzymes or alter the cell’s genetic encoding by creating new proteins (called genetic transcription). Each hormone has unique receptors. Many cells have receptors only for certain hormones, eliciting specific and narrowly focused changes. Only cells in the TESTES and OVARIES, for example, have receptors for FOLLICLE-STIMULATING HORMONE (FSH) and LUTEINIZING HORMONE (LH). Some hormones, such as GROWTH HORMONE (GH), have receptors in all cells, in which case the hormone has widespread actions.

Some hormones stimulate and others inhibit activity. Most hormonal responses occur in cascades, with multiple activities resulting from the hormone’s release. For example, the HYPOTHALAMUS releases GROWTH HORMONE—RELEASING HORMONE (GHRH), which stimulates the PITUITARY GLAND to release GH. Growth hormone initiates metabolic changes within some cells, such as the BONE and MUSCLE, and also activates the production of insulinlike growth factors (IGFs) that induce metabolic activity in other cells.

Peptide Hormones

Peptide hormones consist of amino acid chains and are the most abundant form of endogenous hormone. Scientists further define peptide hormones as small peptide (fewer than 10 amino acids), polypeptide (more than 10 and fewer than 100 amino acids), or protein (100 or more amino acids), depending on the length and configuration of the amino acid chain. These distinctions influence the hormone’s mechanisms of action, stability, and receptor binding. Most of the body’s hormones are peptide hormones.

Peptide hormones are water soluble and travel through the bloodstream attached to protein molecules called protein carriers. These larger structures keep the hormone intact during transit. Most peptide hormones cannot penetrate the wall of the cell. Instead, they bind with protein receptors on the cell’s surface (also called the plasma membrane).

The binding causes a chemical reaction that activates proteins within the cell that then carry the hormone’s message within the cell, indirectly influencing cell activity. Among the exceptions are the thyroid hormones, which do cross the cell membrane to bind with receptors in the cell nucleus and directly influence the cell’s activity.

PEPTIDE HORMONES

ANTIDIURETIC HORMONE (ADH)	CALCITONIN
cholecystokinin (CCK)	CHORIONIC GONADOTROPIN
CORTICOTROPIN-RELEASING HORMONE (CRH)	enterogastrone
gastric inhibitive polypeptide (GPI)	FOLLICLE-STIMULATING HORMONE (FSH)
GLUCAGON	gastrin
GROWTH HORMONE (GH)	GONADOTROPIN-RELEASING HORMONE (GNRH)
GROWTH HORMONE—RELEASING HORMONE (GHRH)	INHIBIN
LUTEINIZING HORMONE (LH)	INSULIN
motilin	MELATONIN
PARATHYROID HORMONE	OXYTOCIN
RELAXIN	PROLACTIN
secretin	RENIN
THYROID-STIMULATING HORMONE (TSH)	SOMATOSTATIN
THYROXINE (T ₄)	THYROTROPIN-RELEASING HORMONE (TRH)
vasoactive intestinal peptide (VIP)	TRIIODOTHYRONINE (T ₃)

Steroid Hormones

Steroid hormones are lipid structures that derive from cholesterol. Scientists further define steroid hormones as corticosteroids (glucocorticoids and mineralocorticoids), sex steroids (ANDROGENS, ESTROGENS, PROGESTERONE), and vitamin D derivatives. Like peptide hormones, steroid hormones bind to protein carriers to transport them through the bloodstream to their target cells. Steroid hormones penetrate the wall of the cell to bind with receptors (specialized proteins) within the cytoplasm or cell nucleus to directly alter the cell’s activity. Steroid hormones elicit genetic transcription responses in the cells that contain their receptors.

ENDOGENOUS STEROID HORMONES

ALDOSTERONE	CORTISOL	ESTROGENS
PROGESTERONE	TESTOSTERONE	vitamin D

Pharmaceutical Hormones

Most of the major endocrine hormones are available as purified extracts or synthesized products for therapeutic supplementation or replacement therapy. Endocrinologists and other doctors prescribe pharmaceutical conditions to treat a wide range of endocrine disorders such as ADDISON'S DISEASE, HYPOTHYROIDISM, and DIABETES. Doctors may also prescribe pharmaceutical hormones for CONTRACEPTION (the birth control pill), to enhance FERTILITY, to slow or prevent OSTEOPOROSIS, and to treat HORMONE-DRIVEN CANCERS such as PROSTATE CANCER, ENDOMETRIAL CANCER, and some forms of BREAST CANCER.

Many hormone supplements are recombinant products genetically engineered in laboratories to precisely match the chemical configurations of endogenous (native to the human body) hormones. Some hormone products contain purified extracts drawn from animal sources, most commonly human (extracted from donor cadaver organs), porcine (pig) and bovine (cow). Most people can tolerate either type of supplement, though adverse reactions (including allergic responses) tend to be more common with extracts.

For further discussion of hormones within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ANABOLIC STEROIDS AND STEROID PRECURSORS; DIGESTIVE ENZYMES; DIGESTIVE HORMONES; ENDOCRINE GLAND; HORMONE THERAPY.

hormone therapy Treatment in which a person takes HORMONE extracts or synthetic hormones to influence the body's natural production of hormones or to replace hormones the body is no longer producing. Nearly all of the body's major hormones are available as purified extracts, laboratory-synthesized pharmaceuticals, or recombinant products. Common hormone therapy regimens include replacement supplements to treat:

- ACROMEGALY
- ADDISON'S DISEASE
- ADRENAL INSUFFICIENCY
- DIABETES
- GROWTH HORMONE DEFICIENCY

- HYPOPARATHYROIDISM
- HYPOPITUITARISM (especially following treatment for adenoma)
- HYPOTHYROIDISM

Hormone therapy may also be a treatment approach for HORMONE-DRIVEN CANCERS such as PROSTATE CANCER, some BREAST CANCERS, and ENDOMETRIAL CANCER (cancer of the UTERUS). Doctors may also prescribe short-term hormone replacement therapy (HRT) for moderate to severe symptoms related to MENOPAUSE. FERTILITY treatments typically involve hormone therapy to stimulate OVULATION in women or SPERM production in men.

CHANGE IN HRT PRACTICES

For the latter half of the 20th century doctors routinely prescribed moderate doses of ESTROGENS and progestins for women going through and beyond MENOPAUSE, based on the presumption that such hormone replacement therapy (HRT) protected women from heart disease and OSTEOPOROSIS. Several large studies in the early 2000s disproved this premise, establishing concern that routine HRT increased the risk for heart disease as well as HORMONE-DRIVEN CANCERS. Doctors now prescribe small doses of these hormones for short periods of time and only for women who are experiencing moderate to severe symptoms such as hot flashes and sleep disturbances.

See also CANCER TREATMENT OPTIONS AND DECISIONS; OSTEOPOROSIS.

hydrocortisone See CORTISOL.

hyperaldosteronism A condition, also called aldosteronism, in which the adrenal cortex of the ADRENAL GLANDS produces excessive ALDOSTERONE. This causes the KIDNEYS to withhold higher amounts of sodium in the BLOOD and pass into the URINE greater amounts of potassium, which consequently draws greater amounts of water into the blood. The aldosterone also causes the peripheral arterioles (tiny arteries in the CAPILLARY BEDS) to constrict. The combined effect is elevated BLOOD PRESSURE along with an imbalance between sodium and potassium. This imbalance causes disturbances

of the HEART's rhythm (ARRHYTHMIA) that can have serious consequences.

The most common cause of hyperaldosteronism is an ADENOMA (a noncancerous tumor) that grows in the zona glomerulosa, the region of the adrenal cortex that produces aldosterone. Symptoms may appear gradually or rapidly depending on the location and rate of growth of the adenoma. In addition to HYPERTENSION (high blood pressure) and arrhythmias, symptoms may include HEADACHE and fatigue. Some people also experience weakness or dizziness, a potential consequence of arrhythmias.

The diagnostic path includes blood tests to measure the levels of aldosterone and potassium, imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN OR MAGNETIC RESONANCE IMAGING (MRI) to determine the presence of an adrenal tumor, and ELECTROCARDIOGRAM (ECG) to detect and evaluate any arrhythmias. Treatment is surgery to remove the tumor, when possible. The endocrinologist may also prescribe medications such as the potassium-sparing diuretic spironolactone, which works by suppressing aldosterone secretion, in conjunction with a low-sodium diet to help control symptoms either in lieu of surgery or after surgery if the hypertension persists.

Hyperaldosteronism may also develop as a secondary condition resulting from severe CARDIOVASCULAR DISEASE (CVD) such as uncontrolled hypertension or HEART FAILURE. Treatment when this is the case targets the underlying condition and often also incorporates similar dietary restrictions and medications to those prescribed for primary hyperaldosteronism.

See also [ADDISON'S DISEASE](#); [ADRENAL INSUFFICIENCY](#); [CUSHING'S SYNDROME](#).

hypercalcemia A circumstance of excessive calcium in the BLOOD circulation. The most common cause of hypercalcemia is HYPERPARATHYROIDISM (excessive secretion of PARATHYROID HORMONE). Other causes include HYPERTHYROIDISM (overactive THYROID GLAND), long-term therapy with lithium (treatment for BIPOLAR DISORDER) or thiazide diuretics ("water pills"), excessive vitamin D or vitamin A consumption, excessive consumption of calcium carbonate (a form of antacid often taken as a calcium supplement), and some cancers, notably metastatic BONE CANCER.

Hypercalcemia occurs when the bones release excessive calcium into the BLOOD circulation. The loss of calcium weakens the structure of the bones, causing symptoms similar to OSTEOPOROSIS such as BONE PAIN and, when calcium loss is severe, spontaneous fractures. However, hypercalcemia is likely to cause other, more apparent symptoms before the calcium loss reaches such a point.

Calcium is essential for MUSCLE contractions and for the conduction of NERVE impulses, an especially critical combination in the HEART. Hypercalcemia may cause ARRHYTHMIAS (irregularities in the HEART RATE), which are apparent with ELECTROCARDIOGRAM (ECG), and HYPERTENSION (high BLOOD PRESSURE). Hypercalcemia also often has neurologic symptoms as well, such as confusion and cognitive dysfunction, because the excessive calcium in the blood disrupts nerve communication in the BRAIN.

The diagnostic path begins with blood tests to measure calcium and parathyroid hormone levels in the blood. The doctor may conduct an ECG to evaluate any cardiovascular symptoms, and X-rays Or bone scan to assess BONE DENSITY loss or the presence of tumors, particularly in people who have or have been treated for LYMPHOMA, LEUKEMIA, MULTIPLE MYELOMA, OR CARCINOMA. People who have received RADIATION THERAPY to the neck, such as to treat THYROID CANCER OR HYPERTHYROIDISM, are vulnerable to parathyroid ADENOMA (noncancerous tumor of a parathyroid gland) or hyperparathyroidism.

Treatment depends on the severity of the hypercalcemia and any underlying causes. Mild to moderate hypercalcemia may improve with increased HYDRATION in combination with medications that suppress the release of calcium from the bones or the diuretic medication furosemide (Lasix), which blocks the KIDNEYS from reabsorbing calcium from the blood. When the cause is hyperparathyroidism, the most viable treatment option may be surgery to remove the parathyroid glands. When hypercalcemia results from benign causes, treatment usually resolves the situation and blood calcium levels return to normal.

See also [CALCITONIN](#); [MULTIPLE ENDOCRINE NEOPLASIA \(MEN\)](#); [NEPHROLITHIASIS](#); [PHEOCHROMOCYTOMA](#).

hyperkalemia A circumstance of elevated potassium in the BLOOD circulation. The most common

cause of hyperkalemia is kidney dysfunction in which the KIDNEYS retain excessive potassium in the blood. Such dysfunction may develop as a consequence of RENAL FAILURE or due to endocrine disorders such as ADRENAL INSUFFICIENCY. Hyperkalemia may develop in people who have poorly controlled DIABETES as a consequence of chronically elevated blood GLUCOSE levels, which damages kidney function. Sometimes potassium-sparing diuretic medications, which doctors may prescribe to treat HEART FAILURE OR HYPERTENSION (high BLOOD PRESSURE), can result in hyperkalemia. Moderate to severe hyperkalemia causes ARRHYTHMIA (disturbance of the heartbeat).

Weakness and tiredness are the most common symptoms. The diagnostic path includes blood tests to measure the level of potassium and other electrolytes in the blood and ELECTROCARDIOGRAM (ECG) to evaluate the HEART'S electrical activity. Treatment consists of appropriate methods to reduce potassium levels according to the underlying cause. Such methods may include changing medications or doses for diuretics, HORMONE THERAPY to supplement adrenal function, reducing consumption of foods high in potassium (such as bananas, green leafy vegetables, and raisins), or therapies to improve kidney function. Most people who have uncomplicated hyperkalemia fully recover with appropriate treatment.

See also [ADRENAL GLANDS](#); ALDOSTERONE; HYPERALDOSTERONISM.

hypernatremia A circumstance of elevated sodium in the BLOOD circulation. The most common cause of hypernatremia is DEHYDRATION that results from prolonged NAUSEA and VOMITING. Rarely, hypernatremia results from DIABETES INSIPIDUS or other dysfunctions of ANTIDIURETIC HORMONE (ADH) release from the HYPOTHALAMUS or PITUITARY GLAND that causes the KIDNEYS to increase the amount of water they pass from the body. The concentration of sodium in the blood correspondingly rises.

The primary symptom of hypernatremia is extreme thirst. As the concentration of sodium increases symptoms become neurologic and include confusion and seizures. The diagnostic path starts with blood tests to measure sodium and other electrolyte levels in the blood and may

include a water-deprivation test, which measures the body's endocrine responses (such as increased ADH release) to the shift in electrolyte concentrations. Treatment is increased fluid to restore the appropriate water-sodium balance in the blood. When the cause is diabetes insipidus or other ADH-related insufficiency (such as pituitary dysfunction), treatment typically incorporates HORMONE THERAPY with ADH supplement.

See also [ADENOMA](#); [HYPERCALCEMIA](#); [HYPOKALEMIA](#).

hyperparathyroidism A condition in which the PARATHYROID GLANDS secrete an excessive amount of PARATHYROID HORMONE. The four tiny parathyroid glands are on the back of the THYROID GLAND. Parathyroid hormone regulates the balance of calcium and phosphorus in the BLOOD. Excessive parathyroid hormone results in too much calcium pulled from the bones and absorbed from the gastrointestinal tract into the BLOOD circulation (HYPERCALCEMIA). At the same time blood levels of phosphorus drop (hypophosphatemia). Phosphorus helps retain calcium in the bones and is important for BONE STRENGTH. Calcium is also essential for the conduction of NERVE impulses and for MUSCLE contraction. Excessive calcium in the blood disrupts neuromuscular functions.

The most common cause of hyperparathyroidism is an ADENOMA (noncancerous tumor) of a parathyroid gland. Sometimes the parathyroid glands enlarge (parathyroid HYPERPLASIA) without apparent cause. Either circumstance results in increased secretion of parathyroid hormone. Symptoms of hyperparathyroidism tend to be nonspecific and include

- weakness and rapid tiring with physical exertion
- loss of APPETITE
- lethargy and fatigue
- generalized aches and discomforts

OSTEOPOROSIS may be the first indication of hyperparathyroidism in many people. Sometimes conditions such as HYPERTENSION (high BLOOD PRESSURE), a consequence of calcium's actions, or kidney stones (NEPHROLITHIASIS) reveal the underlying cause to be hyperparathyroidism. The diagnostic path includes blood tests to measure the levels of

calcium, phosphorus, and parathyroid hormone in the blood circulation. Further diagnostic procedures to determine the cause of the hyperparathyroidism may include ULTRASOUND of the neck to evaluate the parathyroid glands, as well as tests of kidney function and X-rays to evaluate bone structure and density. Treatment for parathyroid adenoma or parathyroid hyperplasia typically involves surgery to remove the affected parathyroid gland, which permanently ends the oversecretion. Most people recover fully and without residual consequences unless osteoporosis has become significant and requires subsequent treatment.

See also **CALCITONIN**; HYPOPARATHYROIDISM; PAGET'S DISEASE OF THE BONE; SURGERY BENEFIT AND RISK ASSESSMENT.

hyperprolactinemia A circumstance of elevated PROLACTIN in the BLOOD circulation that occurs when the anterior lobe of the PITUITARY GLAND secretes excessive prolactin. One of the most common causes of hyperprolactinemia is HYPOTHYROIDISM (underactive THYROID GLAND). Hypothyroidism causes the HYPOTHALAMUS to increase THYROTROPIN-RELEASING HORMONE (TRH) secretion in an attempt to increase the thyroid gland's production of thyroid hormones. TRH also stimulates the pituitary gland to release prolactin. Hyperprolactinemia may also result from a prolactin-secreting ADENOMA of the pituitary gland, a noncancerous tumor also called a prolactinoma. Numerous medications may interfere with the endocrine cascades by suppressing DOPAMINE, a HORMONE that "turns off" prolactin secretion.

Hyperprolactinemia has both direct action and cascading effects on the endocrine function. The direct action of prolactin activates the milk ducts in the breasts, causing milk production and lactation. The cascading effects begin with the hypothalamus and carry through the endocrine cascade to the gonads (sex glands). Elevated levels of prolactin in the blood circulation shut off the hypothalamus's production of GONADOTROPIN-RELEASING HORMONE (GNRH), which consequently slows the pituitary gland's production of LUTEINIZING HORMONE (LH) and FOLLICLE-STIMULATING HORMONE (FSH). These events further lead to reduced production of ESTROGENS, PROGESTERONE, and TESTOSTERONE by the OVARIES, TESTICLES, and ADRENAL GLANDS.

In women the primary symptoms of hyperprolactinemia include disturbances of MENSTRUATION (notably infrequent or absent menstrual periods), INFERTILITY, and milk production (galactorrhea) when not pregnant or BREASTFEEDING. In men the primary symptoms of hyperprolactinemia include ERECTILE DYSFUNCTION and HYPOGONADISM resulting from diminished testosterone levels. When the cause of the hyperprolactinemia is a prolactinoma, both men and women may experience headaches and disturbances of vision from pressure the tumor applies on adjacent structures, such as the OPTIC NERVE, in the BRAIN.

The diagnostic path begins with blood tests to measure the levels of key hormones such as the thyroid hormones, the sex hormones, and prolactin. The results of these tests determine the further course of diagnostic procedures, which may include MAGNETIC RESONANCE IMAGING (MRI) of the head to evaluate the possibility of prolactinoma or ULTRASOUND of the neck to assess the thyroid gland. Treatment targets the underlying cause of the excessive prolactin secretion, which may require surgery to remove an adenoma or medications (dopamine agonists, which suppress prolactin secretion) to treat prolactinoma, or hormone replacement therapy to treat hypothyroidism. Most people recover fully and without residual consequences after appropriate treatment, though may require ongoing treatment for the identified underlying conditions.

See also HYPOPITUITARISM; OSTEOPOROSIS; SURGERY BENEFIT AND RISK ASSESSMENT.

hyperthyroidism A condition, also called thyrotoxicosis, in which the THYROID GLAND overproduces thyroid hormones. The excessive thyroid hormones accelerate METABOLISM.

In health the endocrine system maintains a precise balance among the thyroid hormones to regulate many of the functions of metabolism. The thyroid hormonal cascade begins when the HYPOTHALAMUS produces THYROTROPIN-RELEASING HORMONE (TRH). TRH stimulates the anterior lobe of the PITUITARY GLAND to release THYROID-STIMULATING HORMONE (TSH). TSH stimulates the thyroid gland to synthesize TRIIODOTHYRONINE (T₃) and THYROXINE (T₄), the major active thyroid hormones, as well as several minor or precursor (inactive) thyroid hormones.

When T_3 and T_4 reach appropriate levels in the BLOOD circulation, the hypothalamus ceases TRH production and the thyroid hormone cascade tapers off.

Hyperthyroidism may result from a dysfunction of the thyroid hormone cascade (usually a failure of the pituitary gland to appropriately produce TSH) or overactivity of the thyroid gland. Pituitary ADENOMA is the most common cause of TSH-based hyperthyroidism. Pituitary adenomas secrete TSH that is more potent than normal TSH, eliciting a stronger response from the thyroid gland. Hyperthyroidism that arises from overactivity of the thyroid gland may have various causes. Among them are

- GRAVES'S DISEASE, an autoimmune disorder in which the IMMUNE SYSTEM produces antibodies that attack thyroid tissue
- damage to the thyroid gland resulting from radiation exposure (including RADIATION THERAPY involving structures of the neck, lower face, or upper chest)
- thyroid nodules (nearly always noncancerous)
- excessive consumption of iodine, often resulting from medications that contain iodine (such as the antiarrhythmia medication amiodarone)
- THYROIDITIS (INFLAMMATION of the thyroid gland)
- excessive consumption of therapeutic thyroid hormone supplements (also called thyrotoxicosis factitia)
- THYROID CANCER, which is rare

A dangerous weight loss practice is the intentional consumption of thyroid hormone supplement by people who have normal thyroid function. Though this accelerates METABOLISM to generate weight loss, the resulting state of hyperthyroidism can cause serious disturbances of the HEART'S rhythm (ARRHYTHMIA) and the life-threatening condition THYROID STORM, which requires emergency medical treatment. Only people with diagnosed HYPOTHYROIDISM (underactive thyroid) should take thyroid hormone supplement, and only at the DOSE the doctor prescribes.

Symptoms and Diagnostic Path

Hyperthyroidism tends to develop over weeks to months with few indications until thyroid HORMONE levels become significantly elevated, such that the condition may be quite advanced by the time the person becomes aware of symptoms. The most common symptoms of hyperthyroidism are

- racing PULSE and PALPITATIONS
- weight loss
- feeling hot and intolerance to environmental heat
- moist, warm SKIN
- irritability, anxiety, and insomnia (difficulty sleeping)

GOITER (enlarged thyroid gland) is common. People who have Graves's disease may also have EXOPHTHALMOS (bulging eyes, also called proptosis) and autoimmune symptoms involving the SKIN and other body systems. The diagnostic path begins with blood tests to measure the levels of the thyroid hormones in the blood circulation. In hyperthyroidism that originates with the thyroid gland, T_3 and T_4 are usually elevated and TSH is lower than normal. When there is a dysfunction of TSH or the thyroid hormone cascade, T_3 and T_4 are elevated and TSH is normal. Further diagnostic procedures to determine the cause of the hyperthyroidism may include ULTRASOUND or radioiodine scan (also called radioactive-reuptake scan) of the neck to detect nodules or inflammation of the thyroid gland.

Treatment Options and Outlook

Treatment targets reducing thyroid hormone production. Such an approach may include antithyroid medications, radioactive iodine, or surgery to remove part or all of the thyroid gland. The appropriate treatment depends on the circumstances of the hyperthyroidism and the person's overall health status. Antithyroid medications, commonly methimazole and propylthiouracil (PTU), work by interfering with thyroid hormone synthesis and with conversion of T_4 to T_3 . Antithyroid medication therapy must be continuous; most people experience a return of hyperthyroidism when they stop taking the medications.

Radioactive iodine, ^{131}I , which destroys thyroid tissue, and surgery to remove part or all of the

thyroid gland provide permanent solutions to thyroid hormone overproduction. Most people subsequently require long-term thyroid hormone supplements (HORMONE THERAPY) to maintain adequate thyroid hormone levels in the blood, as these treatments often leave the thyroid gland incapable of synthesizing thyroid hormones. Total thyroidectomy always requires thyroid hormone replacement.

When the hyperthyroidism is likely transitory, as with thyroiditis, treatment may target only symptom relief because thyroid function will return to normal when the inflammation subsides. Beta blocker medications (notably propranolol) relieve the symptoms that are the most distressing—palpitations, irritability, and heat insensitivity. Endocrinologists also sometimes prescribe beta blockers in conjunction with antithyroid therapies when these symptoms cause pronounced discomfort, until thyroid function returns to normal.

A life-threatening complication of untreated hyperthyroidism is THYROID STORM, in which there are extensive cardiovascular and NERVOUS SYSTEM responses to the elevated thyroid hormone levels. Often, thyroid storm manifests in a person who is unaware of having hyperthyroidism who develops another health condition that stresses the body. Congestive HEART FAILURE, serious arrhythmias, and cardiovascular SHOCK can develop very rapidly and require emergency medical treatment.

Risk Factors and Preventive Measures

Exposure to radiation and excessive iodine consumption are the primary known risk factors for hyperthyroidism. People who have other AUTOIMMUNE DISORDERS are more likely to develop Graves's disease. The only preventable forms of hyperthyroidism are those which result from overconsumption of thyroid-hormone supplements and medication therapies that result in excessive iodine consumption. Otherwise, there are no known measures for preventing hyperthyroidism.

See also GRAVES'S OPHTHALMOPATHY; HYPOTHYROIDISM.

hypoadrenocorticism See ADDISON'S DISEASE.

hypocalcemia A circumstance of insufficient calcium in the BLOOD circulation. Common causes

of hypocalcemia include chronic DIARRHEA, which prevents calcium absorption from dietary sources, and lack of sun exposure, which prevents activation of vitamin D (crucial for calcium absorption). HYPOPARATHYROIDISM is the most common endocrine cause for hypocalcemia, and may result from atrophy, dysfunction, or surgical removal of the PARATHYROID GLANDS. Some people develop resistance to PARATHYROID HORMONE, usually as a consequence of vitamin D deficiency.

Calcium is essential for many functions within the body, notably the conduction of NERVE impulses and MUSCLE contractions. Inadequate calcium in the blood disrupts these functions and may result in ARRHYTHMIA (irregular HEART RATE), HYPOTENSION (low BLOOD PRESSURE), mental confusion and irritability, and muscle spasms (tetany). Severely low levels of calcium in the blood can cause seizures, and prolonged hypocalcemia can result in PAPILLEDEMA (swelling where the OPTIC NERVE exits the RETINA) and permanent damage to the CORNEA.

The diagnostic path includes blood tests to measure the levels of calcium and parathyroid hormone in the blood, a comprehensive NEUROLOGIC EXAMINATION, and an ELECTROCARDIOGRAM (ECG) to assess any irregularities in the functioning of the HEART. Other diagnostic procedures may include X-rays of the bones, ULTRASOUND, COMPUTED TOMOGRAPHY (CT) scan, or MAGNETIC RESONANCE IMAGING (MRI) to visualize the parathyroid glands. Treatment targets any underlying conditions, then focuses on restoring appropriate calcium balance in the body, typically through dietary changes to increase the amount of calcium in the diet, and with calcium and vitamin D supplements. Most people recover fully and without residual consequences with appropriate treatment. Long-term treatment may be necessary, depending on the cause of the hypocalcemia.

See also CHEMOTHERAPY; FANCONI'S SYNDROME; PANCREATITIS; POLYGLANDULAR DEFICIENCY SYNDROME; SEIZURE DISORDERS.

hypoglycemia A circumstance in which the BLOOD GLUCOSE level is too low. A normal blood glucose level is 70 milligrams per deciliter (mg/dL) to 100 mg/dL. The clinical standard for hypoglycemia is a blood glucose level below 50 mg/dL,

though some people may experience symptoms of hypoglycemia with blood glucose levels between 50 mg/dL and 70 mg/dL.

Hypoglycemia most commonly occurs in people who have DIABETES, manifesting as a consequence of taking more INSULIN or antidiabetes medication than is necessary to balance carbohydrate consumption or due to a more intense level of physical activity than usual, which increases the body's need for glucose. Hypoglycemia also can occur in people who do not have diabetes, often as a result of inadequate carbohydrate consumption particularly during intense physical exercise or with extended fasting (going without food). Excessive ALCOHOL consumption, particularly in people who have CIRRHOSIS of ALCOHOLISM or other LIVER disease, may also cause hypoglycemia. An uncommon form of nondiabetes hypoglycemia is reactive hypoglycemia, in which the blood glucose level drops within three to four hours after eating. Researchers do not know what causes reactive hypoglycemia.

Imbalances or dysfunctions of the endocrine system's hormonal cascades may slow the body's efforts to restore adequate blood glucose levels. In health, a low blood glucose level triggers the ISLETS OF LANGERHANS to release GLUCAGON, which directs the liver to convert glycogen (a storage form of glucose) to glucose. Simultaneously, the HYPOTHALAMUS releases CORTICOTROPIN-RELEASING HORMONE (CRH) and GROWTH HORMONE-RELEASING HORMONE (GHRH), which set in motion hormonal cascades to alter METABOLISM in ways that slow the body's use of glucose.

The symptoms of hypoglycemia include

- feeling weak and shaky
- hunger
- excessive sweating
- drowsiness and confusion
- acting intoxicated
- dizziness and lightheadedness

People who have diabetes should check their blood glucose levels at the onset of any of these symptoms. Immediate treatment generally resolves the symptoms, and may include drinking a glass of juice or soda (regular, not diet or sugar-

free products), eating a spoonful of sugar or honey, or eating a small amount of candy. The doctor may follow up with diagnostic tests to determine the cause of the hypoglycemic episode, such as blood tests to measure glucose levels during symptoms. The body's needs for insulin and glucose vary with physical activity, so people who have diabetes may need to adjust their medication doses if they increase their exercise levels and experience repeated episodes of hypoglycemia. Eating small meals frequently (every three hours) maintains a more consistent level of glucose in the blood circulation and is the therapeutic approach doctors recommend for people who have reactive hypoglycemia. Though untreated hypoglycemia can have significant consequences including coma and death, most people respond quickly to treatment and recover without residual effects.

See also [INSULIN RESISTANCE](#).

hypokalemia A circumstance of low potassium in the BLOOD circulation. There are many causes of hypokalemia. Among the most common are persistent DIARRHEA (which depletes electrolytes from the body), long-term therapy with diuretic medications (many of which cause the KIDNEYS to excrete potassium), and kidney disease (which affects the ability of the kidneys to regulate potassium retention). Endocrine causes for hypokalemia include HYPERALDOSTERONISM (oversecretion of ALDOSTERONE) and excessive ADRENOCORTICOTROPIN HORMONE (ACTH) such as occurs with CUSHING'S SYNDROME.

The symptoms of hypokalemia are those of electrolyte imbalance. Mild to moderate symptoms may include MUSCLE weakness or cramping, fatigue, and excessive thirst. Significant hypokalemia can cause confusion, disorientation, and ARRHYTHMIA (irregular heartbeat). Without treatment hypokalemia has the potential to be fatal as it can result in HEART ATTACK OR PARALYSIS of the muscles that impairs BREATHING.

The diagnostic path begins with blood tests that measure the levels of potassium, sodium, magnesium, and other electrolytes in the blood. An ELECTROCARDIOGRAM (ECG) identifies any arrhythmias. Treatment is potassium supplementation, which may need to be intravenous when symptoms are severe. Potassium tablets (as the doctor prescribes)

or foods high in potassium such as bananas, oranges, potatoes, and green leafy vegetables can provide adequate potassium supplementation for mild to moderate hypokalemia.

See also [FANCONI'S SYNDROME](#); [HYPERKALEMIA](#); [MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE](#); [RENAL FAILURE](#).

hyponatremia A circumstance of insufficient sodium in the BLOOD circulation. Hyponatremia is a symptom of numerous underlying health conditions rather than itself a disorder. The most common cause of hyponatremia is DEHYDRATION, typically as a consequence of extended VOMITING and DIARRHEA or of diuretic therapy (medications taken to reduce the volume of fluid in the body, many of which work by causing the KIDNEYS to increase the amount of sodium they pass from the body in the URINE). Among the endocrine conditions that cause hyponatremia are HYPOTHYROIDISM, ADRENAL INSUFFICIENCY, ADDISON'S DISEASE, and hypoaldosteronism. Nonendocrine systemic disorders that can cause hyponatremia include NEPHROTIC SYNDROME, RENAL FAILURE, CIRRHOSIS, LIVER FAILURE, and congestive HEART FAILURE.

Mild hyponatremia may show no symptoms, with the doctor making the detection during blood tests done for various reasons to measure electrolyte levels. Moderate to severe hyponatremia has primarily neurologic symptoms, as the imbalance between sodium and water in the BRAIN affects communication among neurons (NERVE cells). Symptoms include confusion, cognitive dysfunction, and changes in mood or personality. The diagnostic path typically includes blood tests to measure the amounts of sodium and other electrolytes in the blood, urinalysis to measure the proportions of excreted electrolytes to water, and appropriate tests and procedures to evaluate any suspected endocrine or other health conditions that could be responsible for the hyponatremia.

Hyponatremia requires prompt medical treatment to restore the sodium balance in the blood circulation. Often, identifying and targeting the underlying cause (such as reducing the DOSE of a diuretic medication or hormone supplementation therapy to restore hormonal balance) brings about homeostasis. Untreated hyponatremia can lead to cerebral edema (swelling in the brain), loss of con-

sciousness, and death. When the cause is endocrine dysfunction, such as hypothyroidism or Addison's disease, lifelong HORMONE THERAPY is typically necessary. Many people fully recover from hyponatremia though may need ongoing medical treatment for the underlying health condition.

See also [ALCOHOLISM](#); [COGNITIVE FUNCTION AND DYSFUNCTION](#); [HYPERNATREMIA](#); [MALNUTRITION](#); [MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE](#).

hypoparathyroidism A rare condition in which the amount of PARATHYROID HORMONE in the BLOOD circulation is insufficient, as a consequence of either dysfunction or absence of the PARATHYROID GLANDS. Thyroidectomy (surgical removal of the THYROID GLAND, such as to treat THYROID CANCER) is the most common reason for absence of the parathyroid glands, as the four parathyroid glands rest on the back surface of the thyroid gland. Occasionally the parathyroid glands are the target of an autoimmune attack that destroys their ability to function. Rarely, the parathyroid glands are absent from birth, a congenital anomaly that requires lifelong calcium and vitamin D supplement therapy to maintain adequate blood calcium levels as well as BONE STRENGTH and density.

Hypoparathyroidism results in inadequate calcium (HYPOCALCEMIA) and excessive phosphorus (hyperphosphatemia) in the blood. The symptoms of hypoparathyroidism are those of hypocalcemia and may include

- tingling of the toes, fingers, and lips
- MUSCLE cramps
- rarely, seizures

The diagnostic path includes blood tests to measure the levels of calcium, phosphate, and parathyroid hormone in the blood circulation. Treatment for confirmed hypoparathyroidism is supplementation with calcium and vitamin D. When the parathyroid glands are missing or destroyed, lifelong treatment is necessary.

See also [HYPERCALCEMIA](#); [HYPERPARATHYROIDISM](#); [MINERALS AND HEALTH](#); [OSTEOPOROSIS](#); [VITAMINS AND HEALTH](#).

hypopituitarism A condition in which the PITUITARY GLAND secretes an insufficient amount of one

or more of the hormones it produces. There are numerous causes for hypopituitarism, some of which are transient and others that require lifelong HORMONE THERAPY to supplement hormone deficiencies. Tumors, INFECTION, trauma, and AUTOIMMUNE DISORDERS are the most common causes of pituitary damage resulting in hypopituitarism. AMYLOIDOSIS and SARCOIDOSIS may also cause hypopituitarism. Occasionally the deficiencies result from damage to the HYPOTHALAMUS, which regulates pituitary function, or to the communication between the hypothalamus and the pituitary gland. Deficiencies may involve any of the hormones the anterior lobe of the pituitary gland synthesizes.

The diagnostic path includes BLOOD tests to measure HORMONE levels. The endocrinologist may choose to conduct diagnostic imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) to evaluate the structural integrity of the involved endocrine glands. Treatment consists of appropriate hormone therapy, usually lifelong, to supplement deficient hormones.

See also [HYPERPROLACTINEMIA](#); [POLYGLANDULAR DEFICIENCY SYNDROME](#).

hypothalamus A structure of the midbrain that has both neurologic and endocrine functions, serving as a bridge between the neurologic system

and the endocrine system. A construction of primarily NERVE cells, the hypothalamus receives and processes myriad signals from the BRAIN and central NERVOUS SYSTEM about vital functions such as BREATHING, HEART RATE, BLOOD PRESSURE, body temperature (thermoregulation), and fluid balance. In response to these neurologic signals specific centers in the hypothalamus synthesize (produce) numerous hormones that direct the PITUITARY GLAND to secrete or stop secreting the hormones it synthesizes or stores.

A dedicated network of BLOOD vessels connects the hypothalamus and the pituitary gland, which lies beneath the hypothalamus, allowing hypothalamic hormones to travel through the blood directly to the pituitary gland and fostering intimate and continuous communication between the two structures. In turn, the hormones the pituitary gland produces enter the general circulation to direct the functions of other endocrine glands. Through this cascading hormonal regulation the hypothalamus controls, in integration with neurologic processes, most core functions essential for survival.

Hypothalamic Hormones

The hormones the hypothalamus produces are peptides (amino acid structures) that target specific cell clusters within the pituitary gland's two lobes, acting either to stimulate or inhibit pituitary gland activity. The hypothalamic hormones are

PITUITARY HORMONE DEFICIENCIES	
Deficient Hormone	Consequences
deficient ADRENOCORTICOTROPIN HORMONE (ACTH)	ADRENAL INSUFFICIENCY: HYPOTENSION, HYPOGLYCEMIA, fatigue
deficient GROWTH HORMONE (GH)	children: stunted growth adults: slowed METABOLISM
deficient LUTEINIZING HORMONE (LH) and FOLLICLE-STIMULATING HORMONE (FSH)	women: cessation of OVULATION and MENSTRUAL CYCLES, INFERTILITY, masculinization men: HYPOGONADISM, infertility, ERECTILE DYSFUNCTION, feminization
deficient THYROID-STIMULATING HORMONE (TSH)	HYPOTHYROIDISM: weight gain, confusion, intolerance to cold, chronic CONSTIPATION
deficient PROLACTIN	BREASTFEEDING women: inability to produce milk

- ANTIDIURETIC HORMONE (ADH), which the pituitary gland stores and releases to regulate the amount of water the KIDNEYS retain in the blood as one of the body’s mechanisms for controlling blood pressure
- CORTICOTROPIN-RELEASING HORMONE (CRH), which stimulates the pituitary gland to release ADRENOCORTICOTROPIN HORMONE (ACTH) as the first level in the body’s STRESS RESPONSE HORMONAL CASCADE
- DOPAMINE, which inhibits pituitary gland production of FOLLICLE-STIMULATING HORMONE (FSH), LEUTEINIZING HORMONE (LH), THYROID-STIMULATING HORMONE (TSH), and PROLACTIN
- GONADOTROPIN-RELEASING HORMONE (GNRH), which stimulates the pituitary gland to synthesize and release LH and FSH, hormones that are fundamental to reproduction
- GROWTH HORMONE–RELEASING HORMONE (GHRH), which stimulates the pituitary gland to synthesize and release GROWTH HORMONE (GH)
- OXYTOCIN, which the pituitary gland subsequently stores and releases when needed to stimulate contractions of the UTERUS during CHILDBIRTH and to influence sexual arousal in both men and women
- THYROTROPIN-RELEASING HORMONE (TRH), which stimulates the pituitary gland to synthesize and release TSH, initiating hormonal regulation of vital functions such as thermal regulation and cellular METABOLISM, and to produce prolactin, which stimulates milk production during BREASTFEEDING

Structure of the Hypothalamus

Despite the vital and extensive nature of its functions, the hypothalamus is physically a small structure not quite the size and shape of an almond. Within the hypothalamus are a number of functionally distinct substructures, called nuclei, each having unique and specific roles that require intimate integration with one another. The major nuclei that have endocrine functions are the

- supraoptic nucleus, which synthesizes and releases ADH

- paraventricular nucleus, which synthesizes and releases oxytocin, CRH, and TRH
- arcuate nucleus, which synthesizes and releases GHRH
- suprachiasmatic nucleus (SCN), which influences the circadian cycle and various body rhythms through the cyclic release of certain hormones
- ventromedial nucleus, which regulates APPETITE

Disorders and dysfunctions of the hypothalamus are extremely rare, and when they do occur tumors are the most likely cause. Disorders and dysfunctions of other endocrine glands can affect the ways those glands respond to hypothalamic hormones. Long-term, chronic ALCOHOL abuse destroys hypothalamic cells, affecting the endocrine and neurologic functions of the hypothalamus.

HYPOTHALAMIC HORMONES

ANTIDIURETIC HORMONE (ADH)	CORTICOTROPIN-RELEASING HORMONE (CRH)
DOPAMINE	GROWTH HORMONE–RELEASING HORMONE (GHRH)
GONADOTROPIN-RELEASING HORMONE (GNRH)	SOMATOSTATIN
OXYTOCIN	
THYROTROPIN-RELEASING HORMONE (TRH)	

For further discussion of the hypothalamus within the context of the endocrine system’s structure and function please see the overview section “The Endocrine System.” For further discussion of the hypothalamus within the context of neurologic structures and functions please see the overview section “The Neurologic System.”

See also [ADRENAL GLANDS](#); [OBESITY](#); [PINEAL GLAND](#); [THYMUS](#); [THYROID GLAND](#).

hypothyroidism A condition in which the THYROID GLAND secretes an insufficient amount of thyroid hormones. It is the most common disorder of thyroid function, affecting about 7 million Americans. Women are eight times more likely than men to have hypothyroidism. Risk for hypothyroidism increases among men and women with advancing age. Health experts estimate 80 percent of people over age 70 have hypothyroidism, though the rate of diagnosis is not this high.

The thyroid hormones, primarily THYROXINE (T_4) and TRIIODOTHYRONINE (T_3), regulate METABOLISM in every cell. Deficiencies of these hormones cause numerous symptoms that reflect slowed metabolism. The consequences can be particularly significant when hypothyroidism occurs in children, interfering with physical growth and intellectual development. Congenital hypothyroidism (formerly called cretinism) can cause permanent impairments. Fortunately congenital hypothyroidism is rare in the United States because newborn and well-child health-care screenings test for hypothyroidism.

The follicular cells of the thyroid gland synthesize (manufactures) thyroid hormones from the amino acid tyrosine and the mineral iodine, both of which it acquires from dietary sources. A shortage of either in the diet, though very uncommon in the United States, can impair thyroid hormone synthesis. The hypothalamus initiates the hormonal cascade that results in thyroid hormone production, secreting THYROID-RELEASING HORMONE (TRH) when T_3 and T_4 levels in the BLOOD circulation drop. TRH stimulates the anterior lobe of the PITUITARY GLAND to produce THYROID-STIMULATING HORMONE (TSH), which in turn stimulates the thyroid gland's follicular cells. Rising T_3 and T_4 levels in the blood then reverse the hormonal cascade.

Sometimes the cause of hypothyroidism is clear. Hypothyroidism is certain in anyone who has had a total thyroidectomy (removal of the thyroid gland, such as to treat THYROID CANCER or GRAVES'S DISEASE) and likely in a person who has had a partial thyroidectomy. Treatment for HYPERTHYROIDISM (overactive thyroid gland) often results in eventual hypothyroidism as follicular cells within the thyroid gland continue to die after treatment ends. The most common identifiable cause is THYROIDITIS, an INFLAMMATION of the thyroid gland that destroys follicular cells and that may be an autoimmune process. Most often, however, hypothyroidism is idiopathic—the cause remains unknown.

Symptoms and Diagnostic Path

The symptoms of hypothyroid appear gradually and are often nonspecific. They typically include

- chronic tiredness

- weight gain or inability to lose weight
- DEPRESSION and irritability
- coarsening HAIR and hair loss
- dry, flaky SKIN
- loss of eyebrow hair
- intolerance to cold or feeling cold regardless of the environmental temperature
- irregular MENSTRUATION and INFERTILITY

Some people also have a GOITER, a painless swelling of the thyroid gland that may be visible when looking in the mirror or that the doctor can feel. The diagnostic path begins with blood tests to measure the levels of thyroid hormones in the blood circulation. A low level of T_3 and T_4 coupled with elevated TSH indicates the thyroid gland is not responding to the pituitary gland's hormonal signals and provides a conclusive diagnosis of hypothyroidism. Some people have borderline blood test results though have hypothyroidism nonetheless. When blood thyroid levels are marginal, the doctor may recommend a trial of treatment to see if symptoms improve.

Treatment Options and Outlook

Treatment is HORMONE THERAPY with thyroid hormone supplement to deliver adequate levels of thyroid hormones. The most common form of thyroid hormone supplement is a synthetic pharmaceutical preparation of T_4 (levothyroxine). This provides adequate thyroid hormones for most people because the cells in the body convert T_4 to T_3 when it binds with them. There are several levothyroxine products available. Endocrinologists recommend staying with the same product consistently, as the formulations of each product are somewhat different. Some doctors also prescribe T_3 hormone supplement, which is faster-acting, in combination with a T_4 hormone supplement, as an approach that attempts to more precisely replicate the body's thyroid hormone synthesis. The doctor also may prescribe a short course of T_3 to rapidly bring thyroid hormone levels up when hypothyroidism is severe, then taper off and resume T_4 supplement.

Most people experience some improvement of symptoms within two weeks of starting hormone therapy. However, it may take six months to a

year to establish the most effective DOSE, during which time the doctor will routinely measure the thyroid hormones in the blood and compare them with changes in symptoms and the overall clinical picture. Most people experience a vast improvement within a month of beginning hormone therapy. Treatment is lifelong. Undertreated or untreated hypothyroidism results in progressively worsening symptoms that can culminate in permanent damage to the cardiovascular and neurologic systems. People over age 60 typically need lower doses of thyroid hormone supplement for therapeutic results.

Risk Factors and Preventive Measures

The key risk factors for hypothyroidism are being female and age over 60; being both female and over 60 in combination increases the risk because of estrogen's role in hormone balance. People who have received RADIATION THERAPY to the lower face, neck, or upper chest have increased risk for hypothyroidism. Lithium, a medication taken for BIPOLAR DISORDER, may disrupt thyroid function and cause hypothyroidism. There are no measures to prevent hypothyroidism.

See also AUTOIMMUNE DISORDERS; CALCITONIN; ESTROGENS; EUTHYROID SICK SYNDROME.



inhibin A peptide HORMONE the corpus luteum in ovulating women and the TESTES in men produce that stops the HYPOTHALAMUS from secreting GONADOTROPIN-RELEASING HORMONE (GNRH). This in turn stops the PITUITARY GLAND from secreting LUTEINIZING HORMONE (LH) and FOLLICLE-STIMULATING HORMONE (FSH), halting the subsequent cascade of sex hormones from the gonads (sex glands). Researchers do not yet fully understand the full range of inhibin's actions, though it influences spermatogenesis (SPERM production) in men and likely has additional roles in OVULATION. Some research suggests inhibin may serve as a marker to indicate an emerging OVARIAN CANCER or PROSTATE CANCER. With the cessation of ovulation a woman's OVARIES no longer produces inhibin, so inhibin is no longer present in the BLOOD circulation of post-menopausal women. Inhibin production returns, however, when there is an ovarian cancer. Conversely, inhibin levels appear to drop in men who have BENIGN PROSTATIC HYPERTROPHY (BPH) or prostate cancer.

For further discussion of inhibin within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also [FERTILITY](#); [PREGNANCY](#); [TESTOSTERONE](#).

insulin A peptide HORMONE the ISLETS OF LANGERHANS in the PANCREAS produce that is essential for the body to use GLUCOSE. Insulin has numerous roles in the body, the best known of which is the regulation of glucose levels in the BLOOD (carbohydrate METABOLISM). Glucose, a basic sugar molecule, is a primary energy source for many cellular activities. When insulin binds with insulin receptors on a cell membrane, the cell allows glucose

molecules to enter. Insulin facilitates lipid (fatty acid) metabolism, stimulates the LIVER to convert excess glucose into the intermediary storage form glycogen, and facilitates the conversion of amino acids to proteins for building new MUSCLE tissue. Insulin also participates in cell activities related to growth.

The beta cells of the islets of Langerhans synthesize insulin in response to declining glucose levels in the blood. The release of insulin allows cells to accept glucose and at the same time directs the liver to begin converting glucose to glycogen for storage. Insulin also slows the conversion of fatty acids to glycogen, a process intended to conserve the long-term energy resources of the body (fat). These functions become less efficient in INSULIN RESISTANCE, a condition in which the cells are slow to bind with insulin. Disturbances of insulin sensitivity can allow lipids to accumulate in the blood circulation, contributing to cardiovascular diseases such as ATHEROSCLEROSIS and CORONARY ARTERY DISEASE (CAD). Insufficient insulin production results in DIABETES, for which insulin is available as an injectable pharmaceutical as HORMONE THERAPY. Most forms of insulin available today are recombinant constructions engineered in the laboratory to precisely match the molecular structure and actions of endogenous human insulin.

For further discussion of insulin within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also [CORTISOL](#); [DIGESTIVE ENZYMES](#); [DIGESTIVE HORMONES](#).

insulin resistance A condition, also called metabolic syndrome X or syndrome X, in which the cells

throughout the body do not respond to the normal amounts of INSULIN the ISLETS OF LANGERHANS produce. The short-term result is an excessive level of GLUCOSE in the BLOOD circulation and the need for the islet cells to produce increasing amounts of insulin. Over the long term a constellation of health conditions appears that may include OBESITY, HYPERLIPIDEMIA, type 2 DIABETES, CORONARY ARTERY DISEASE (CAD), HYPERTENSION (high BLOOD PRESSURE), and POLYCYSTIC OVARY SYNDROME (PCOS). Doctors diagnose insulin resistance when a person has two or more of these health conditions.

Treatment must first target the health condition, and may include medications to reduce blood pressure and blood cholesterol levels. CAD may have significant implications for cardiovascular function, and is a major risk for HEART ATTACK as well as HEART FAILURE, CARDIOMYOPATHY, and ISCHEMIC HEART DISEASE (IHD). Weight loss is crucial as OBESITY is a key factor in these conditions as well as in insulin resistance. Lifestyle measures such as nutritious EATING HABITS and daily physical exercise help improve metabolic efficiency and sensitivity to insulin and also aid weight-management efforts. These lifestyle measures practiced consistently over time are often able to reverse some of the health consequences as insulin resistance diminishes, in particular facilitating improvements in obesity, hypertension, and type 2 diabetes.

See also BODY MASS INDEX (BMI); DIABETES AND CARDIOVASCULAR DISEASE; DIET AND HEALTH; EXERCISE AND HEALTH; HEALTH RISK FACTORS; INFERTILITY; LIFESTYLE AND HEALTH; WEIGHT LOSS AND WEIGHT MANAGEMENT.

islets of Langerhans Clusters of endocrine cells distributed throughout the PANCREAS that produce INSULIN, GLUCAGON, and SOMATOSTATIN. There are about a million islet clusters, each containing several hundred islet cells. Each islet contains all three types of islet cells: alpha islet cells, beta islet cells, and delta islet cells.

In the center of each islet are the beta cells, which secrete insulin. Insulin's primary role in the body is the regulation of carbohydrate METABOLISM. Arranged in somewhat of a circle around the core of the islet beta cells are the alpha cells, which

secrete glucagon, and the delta cells, which secrete somatostatin. Glucagon stimulates the LIVER to convert glycogen to GLUCOSE, making more energy available to cells. Somatostatin suppresses the release of GROWTH HORMONE (GH). It also slows the release of insulin and glucagon, as well as the gastrointestinal system's secretion of DIGESTIVE HORMONES.

The most significant disorder affecting the islets of Langerhans is DIABETES. Type 1 diabetes, an autoimmune disorder, destroys the islet cells. Though other cells in the body synthesize the hormones of alpha and delta islet cells—glucagon and somatostatin, respectively—no other cells in the body synthesize insulin. People who have type 1 diabetes must take insulin therapy (injections of pharmaceutical insulin) to meet the needs of their bodies for this crucial hormone. PANCREATITIS, an INFLAMMATION of the pancreas, also can interfere with islet cell functions. Though HORMONE production usually returns when the inflammation subsides, sometimes extensive scarring destroys islet cells, resulting in type 2 (insulin-deficient) diabetes.

For further discussion of the islets of Langerhans within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also AUTOIMMUNE DISORDERS; [DIGESTIVE ENZYMES](#); [POLYGLANDULAR DEFICIENCY SYNDROME](#).

islet cell transplantation An experimental treatment for DIABETES in which the surgeon injects clusters of healthy ISLET OF LANGERHANS cells from a donor (most often a cadaver donor) into the PANCREAS of a person who has type 1 diabetes. Islet cells produce the HORMONE INSULIN as well as two other hormones, GLUCAGON and SOMATOSTATIN. A healthy pancreas contains about a million clusters of islet cells distributed widely throughout the pancreatic tissue. Type 1 diabetes occurs when an autoimmune response destroys the islet cells, eliminating the body's ability to produce insulin. Islet cell transplantation replaces the destroyed cells with healthy islet cells. It may take weeks to months for the transplanted islet cells to establish networks of BLOOD vessels that connect them to the recipient and provide the outlet for the

hormones they produce. At present islet cell transplantation requires subsequent lifelong IMMUNOSUPPRESSIVE THERAPY to prevent rejection of the transplanted cells. Though still experimental, islet

cell transplantation holds considerable promise as a long-term or permanent treatment for type 1 diabetes.

See also ORGAN TRANSPLANTATION.



luteinizing hormone (LH) A peptide HORMONE the anterior lobe of the PITUITARY GLAND produces that stimulates hormonal activity related to reproduction. In men, LH stimulates the development and function of interstitial cells in the TESTES that synthesize and release TESTOSTERONE, the primary male sex hormone. In menstruating women, a mid-menstrual cycle surge of LH stimulates OVULATION (the maturation and release of an ovum, or egg). In a woman who is pregnant, the PLACENTA also produces LH. The HYPOTHALAMUS's release of GONADOTROPIN-RELEASING HORMONE (GNRH) stimulates the pituitary gland to secrete LH. Rising levels of the sex hormones (ESTROGENS, PROGESTERONE, and TESTOSTERONE) and INHIBIN cause the hypothalamus to stop releasing GnHR, ending the pituitary gland's secretion of LH.

For further discussion of LH within the context of the endocrine system's structure and function, please see the overview section "The Endocrine System."

See also ADRENOCORTICOTROPIN HORMONE (ACTH); ANABOLIC STEROIDS AND STEROID PRECURSORS; ANTIDIURETIC HORMONE (AH); [CHORIONIC GONADOTROPIN](#); [FOLLICLE-STIMULATING HORMONE \(FSH\)](#); [GROWTH HORMONE \(GH\)](#); [MENSTRUATION](#); [OXYTOCIN](#); [PROLACTIN](#); [RELAXIN](#); [THYROID-STIMULATING HORMONE \(TSH\)](#).

melatonin A peptide HORMONE that the PINEAL GLAND secretes, the primary function of which is to regulate the body's circadian cycle (pattern of sleep and wake). The pineal gland synthesizes melatonin from the amino acid tryptophan. The OPTIC NERVE appears to convey NERVE messages of outside light and dark from the RETINA to a section of the HYPOTHALAMUS called the suprachiasmatic nucleus (SCN). The SCN sends nerve signals to the

pineal gland, which suspends melatonin synthesis. Darkness causes the nerve messages from the optic nerve to stop, which in turn ends the signals from the SCN. When receiving signals from the SCN, the pineal gland stops melatonin production. When the signals from the SCN end, the pineal gland resumes melatonin production. Researchers believe melatonin causes sleepiness by slowing cell METABOLISM. Other endocrine processes, such as the adrenocorticosteroid hormonal cascade that regulates CORTISOL levels, also slow in conjunction with the circadian cycle, though researchers are uncertain about how these processes may be interrelated.

For further discussion of melatonin within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also MELATONIN SUPPLEMENT; [STRESS RESPONSE HORMONAL CASCADE](#).

multiple endocrine neoplasia (MEN) An inherited genetic disorder in which numerous tumors form in various endocrine glands. Several GENE mutations are responsible for the errant growth of glandular tissue, which may take the form of tumors or hypertrophy (overgrowth). Oversecretion of the affected gland's hormones then occurs. The three forms of MEN are

- MEN-1, in which adenomas develop in the PITUITARY GLAND, PARATHYROID GLANDS, and ISLETS OF LANGERHANS in the PANCREAS
- MEN-2a, characterized by HYPERPARATHYROIDISM, PHEOCHROMOCYTOMA, and medullary THYROID CANCER

- MEN-2b, characterized by pheochromocytoma, neuromas in the mucous membranes of the MOUTH and eyes, and medullary thyroid cancer

The gene MUTATION determines the type of MEN. Not all manifestations occur within each type. Because researchers only identified the gene mutations responsible for MEN in the late 1990s, people who have this autosomal dominant disorder may not realize it runs in their families. Symptoms depend on the endocrine glands affected and the extent of the tumors or hypertrophy. The endocrinologist may suspect MEN based on the patterns of symptoms though GENETIC TESTING is necessary to confirm the mutation. Treatment is surgery to remove the tumors whenever possible, with follow-up CHEMOTHERAPY OR RADIATION THERAPY. Doctors typically recommend prophylactic thyroidectomy for people who carry the gene mutation for MEN-2a or MEN-2b, to head off thyroid cancer as medullary thyroid cancer can be aggressive and is nearly certain to develop. People who have MEN require ongoing medical observation and treatment for hormonal deficiencies that result from therapies for the MEN.

See also GENETIC DISORDERS; INHERITANCE PATTERNS; POLYGLANDULAR DEFICIENCY SYNDROME; ZOLLINGER-ELLISON SYNDROME.

norepinephrine A peptide substance the adrenal medulla of the ADRENAL GLANDS and the synaptic vesicles in the NERVE endings produce. Norepinephrine functions in the body as a HORMONE, when synthesized by the adrenal medulla, and as a NEUROTRANSMITTER when synthesized by BRAIN structures or nerve cells. Norepinephrine is also a DOPAMINE precursor (substance the body uses as the basis for dopamine synthesis). Among the hormones activated in the STRESS RESPONSE HORMONAL CASCADE, norepinephrine acts on the BLOOD vessels

to cause them to constrict (vasoconstriction), helping to raise BLOOD PRESSURE and centralize blood flow. It also facilitates GLYCOGEN conversion to GLUCOSE and lipid METABOLISM, activities related to glucose balance. The HYPOTHALAMUS directs the adrenal medulla, via the neurotransmitter acetylcholine, to release norepinephrine. As a neurotransmitter in the brain, norepinephrine appears to play a role in mood and emotion. Norepinephrine is also available as a pharmaceutical DRUG, used primarily to raise blood pressure in severe HYPOTENSION (low blood pressure) resulting from neurologic causes.

For further discussion of norepinephrine within the context of the endocrine system's structure and function please see the overview section, "The Endocrine System."

See also EPINEPHRINE; SHOCK.

oxytocin A peptide HORMONE the HYPOTHALAMUS synthesizes (produces) and the posterior lobe of the PITUITARY GLAND stores and releases. Oxytocin influences sexual arousal in men and women. In women, oxytocin stimulates uterine contractions during CHILDBIRTH and the milk letdown REFLEX during BREASTFEEDING. Oxytocin may have additional functions in men, including a role in SPERM production. Obstetricians may administer oxytocin as a pharmaceutical DRUG to stimulate uterine contractions to induce labor or to strengthen contractions during childbirth.

For further discussion of oxytocin within the context of the endocrine system's structure and function, please see the overview section "The Endocrine System."

See also ADRENOCORTICOTROPIN HORMONE (ACTH); ANTIDIURETIC HORMONE (ADH); FOLLICLE-STIMULATING HORMONE (FSH); GROWTH HORMONE (GH); LUTEINIZING HORMONE (LH); PROLACTIN; THYROID-STIMULATING HORMONE (TSH).

parathyroid glands Four small endocrine glands, somewhat orange or yellowish in color, normally located in two pairs on the back of each lobe of the **THYROID GLAND**. Sometimes one or more of the parathyroid glands is embedded in the tissue of the thyroid gland, which does not appear to affect either gland's ability to function. Though the thyroid gland and the parathyroid glands are physically connected, they are separate structures with distinct functions. The thyroid gland remains undisturbed if it is necessary to remove any of the parathyroid glands. However, the parathyroid glands have no structure to support them independently and cannot remain if it is necessary to remove the thyroid gland. Absence of all four parathyroid glands requires lifelong **HORMONE THERAPY** with **PARATHYROID HORMONE** supplement.

Occasionally the top two parathyroid glands are located in the neck well above the thyroid gland or the bottom two well below in the chest, a consequence of incomplete migration when the structures separate during fetal development. In the **EMBRYO** the top two parathyroid glands arise from the same tissue as the thyroid gland and the bottom two from the same tissue as the **THYMUS**. Because each parathyroid gland has its own substantial blood supply, its location is not critical for proper function.

For the significance of their function the parathyroid glands are amazingly small, with each gland ranging in size from about that of a grain of rice to that of a small pea. The parathyroid glands produce **parathyroid hormone** (also called **parathormone**), which is essential for proper calcium balance in the body. Calcium is essential for **BONE DENSITY** and **STRENGTH** as well as the conduction of **NERVE** impulses and **MUSCLE** contractions. The parathyroid glands continuously monitor the

level of calcium in the **BLOOD** circulation as blood flows through them. Parathyroid hormone increases the amount of calcium in the blood circulation and exists in dynamic balance with **CALCITONIN**, a hormone the thyroid gland produces that increases the amount of calcium the bones absorb from the blood circulation.

Disorders of the parathyroid glands include **HYPERPARATHYROIDISM** (oversecretion of parathyroid hormone) and **HYPOPARATHYROIDISM** (undersecretion of parathyroid hormone). Either condition may result from hypertrophy (enlargement) of a parathyroid gland or from the development of an **ADENOMA**, a noncancerous tumor. Cancer of the parathyroid glands is very rare. Also rarely a person is born without parathyroid glands, a **CONGENITAL ANOMALY** with significant health consequences.

For further discussion of the parathyroid glands within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also **OSTEOPOROSIS**; **PAGET'S DISEASE OF THE BONE**.

parathyroid hormone A peptide **HORMONE**, also called **parathormone**, the **PARATHYROID GLANDS** secrete that regulates the level of calcium in the **BLOOD** circulation. Parathyroid hormone causes the bones to release calcium into the blood to meet the body's needs. Calcium is essential for the conduction of impulses among nerves and for **MUSCLE** contraction. Calcium helps maintain normal **HEART RATE** and rhythm.

Parathyroid hormone functions in dynamic balance with **CALCITONIN**, a hormone the **THYROID GLAND** produces that lowers blood calcium levels by stimulating the bones to absorb more calcium. Parathyroid hormone also enhances the activation

of vitamin D, increases the amounts of calcium the KIDNEYS retain and the intestines absorb, and increases the amount of phosphorus the kidneys excrete in the URINE.

Long-term excessive parathyroid hormone secretion (HYPERPARATHYROIDISM) leads to OSTEOPOROSIS, a condition in which there is substantial loss of BONE DENSITY and STRENGTH. Inadequate parathyroid hormone secretion (HYPOPARATHYROIDISM) results in disruptions of NERVE impulses and can cause muscle rigidity or cramping.

See also BONE; [HYPERCALCEMIA](#); [HYPOCALCEMIA](#).

pheochromocytoma A neuroendocrine tumor that secretes DOPAMINE, EPINEPHRINE, and NOREPINEPHRINE (collectively called catecholamines). About 90 percent of pheochromocytomas are noncancerous. Most pheochromocytomas develop in the adrenal medulla, the inner structure of the ADRENAL GLANDS, though can occur in other tissues throughout the body. About 10 percent of pheochromocytomas occur in conjunction with MULTIPLE ENDOCRINE NEOPLASIA (MEN), an inherited genetic disorder in which tumors form in numerous endocrine structures. The primary consequence of pheochromocytoma is HYPERTENSION (high BLOOD PRESSURE), which results from the excessive secretion of catecholamines. RETINOPATHY (damage to the RETINA and OPTIC NERVE in the EYE) and CARDIOMYOPATHY (enlarged and weakened HEART) may result with long-term untreated pheochromocytoma.

Symptoms and Diagnostic Path

Symptoms, aside from hypertension, often resemble those of other endocrine disorders, notably HYPERTHYROIDISM. Symptoms of pheochromocytoma may include

- rapid, irregular PULSE (TACHYCARDIA)
- rapid breathing (tachypnea) or shortness of breath (DYSPNEA)
- PALPITATIONS and ARRHYTHMIA (irregularities in the heartbeat)
- orthostatic HYPOTENSION (a sudden drop in blood pressure when rising from a seated or prone position)
- HEADACHE, often severe and persistent
- bouts of NAUSEA and VOMITING
- anxiety and inability to concentrate

The diagnostic path includes blood tests to assess blood electrolyte levels and to rule out more common causes of the symptoms such as hyperthyroidism, ELECTROCARDIOGRAM (ECG) to assess the HEART's electrical activity, and URINE tests to measure the amounts of catecholamine metabolites excreted in the urine. The endocrinologist may also conduct diagnostic imaging procedures such as MAGNETIC RESONANCE IMAGING (MRI) to detect the presence and location of the pheochromocytoma.

Treatment Options and Outlook

Surgery to remove the pheochromocytoma is nearly always the treatment of choice, as nonsurgical therapies are not very successful in controlling the tumor's activities. Adrenergic blocker medications (alpha blockers and beta blockers) can relieve many of the symptoms. Hypotension (low blood pressure) following the tumor's removal is common, with blood pressure gradually returning to normal as the body's production of catecholamines returns to normal. CHEMOTHERAPY follows surgery when the tumor is cancerous. Most people recover fully and without complications after surgery for noncancerous pheochromocytoma, though tumors may recur in people who have MEN. Recovery from malignant pheochromocytoma depends on the extent of METASTASIS.

Risk Factors and Preventive Measures

People who have MEN have significant risk for pheochromocytoma and should be alert to its symptoms. There are no measures to prevent these tumors from developing.

See also [ADRENAL INSUFFICIENCY](#); MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; SURGERY BENEFIT AND RISK ASSESSMENT.

pineal gland A small ENDOCRINE GLAND, about a quarter of an inch long, located within the BRAIN very near the HYPOTHALAMUS. The pineal gland is somewhat cone shaped and reddish in color. It produces MELATONIN, a peptide HORMONE that regulates the body's circadian (sleep-wake) cycle.

Researchers believe the pineal gland produces other hormones and has functions related to immune activity, though what they are remains unknown.

In the philosophies and traditions of Eastern medicine, the pineal gland is the metaphysical “third eye.” Modern researchers have discovered that the pineal gland does in fact receive NERVE signals via the OPTIC NERVE and a structure of the hypothalamus called the suprachiasmatic nucleus (SCN). These signals influence the pineal gland’s synthesis of melatonin, which slows when the external environment is light and accelerates with the external environment is dark.

Dysfunctions of the pineal gland are, as far as endocrinologists know, very rare. Some research has established a link between low melatonin levels and breast cancer, though further research continues to examine this connection. Researchers are also exploring possible connections between pineal function and insomnia (difficulty sleeping).

For further discussion of the pineal gland within the context of the endocrine system’s structure and function please see the overview section “The Endocrine System.”

See also [SLEEP DISORDERS](#).

pituitary gland An ENDOCRINE GLAND located within the BRAIN that secretes the hormones that regulate the activity of the other endocrine structures, except the HYPOTHALAMUS, in the body. A distinctively glandular structure, gray in color and somewhat egg shaped, the pituitary gland nestles into a hollow of BONE at the base of the skull directly beneath the hypothalamus. This physical proximity makes possible a dedicated network of BLOOD vessels that carry hormones from the hypothalamus directly to the pituitary gland, allowing a continuous flow of chemical messages.

The pituitary gland has two lobes, the anterior lobe and the posterior lobe. The posterior lobe stores hormones it receives from the hypothalamus and releases them when hypothalamic signals it to do so. The anterior lobe produces hormones essential for growth and maturation. The hormones of the pituitary gland are peptide hormones. Disorders of the pituitary gland affect FERTILITY, growth, and METABOLISM.

Anterior Lobe Structure and Hormones

The anterior lobe of the pituitary gland, also called the adenohypophysis, is under the hormonal control of the hypothalamus. The hormones the anterior lobe of the pituitary gland synthesizes include

- ADRENOCORTICOTROPIN HORMONE (ACTH), which signals the ADRENAL GLANDS to release CORTISOL, EPINEPHRINE, and NOREPINEPHRINE
- GROWTH HORMONE (GH), which stimulates growth during childhood by increasing the rate at which cells divide and helps maintain MUSCLE mass in adulthood
- THYROID-STIMULATING HORMONE (TSH), which stimulates the THYROID GLAND to release the primary thyroid hormones THYROXINE (T₄) and TRI-iodothyronine (T₃)
- FOLLICLE-STIMULATING HORMONE (FSH), which initiates egg maturation in the OVARIES and SPERM production in the TESTES
- LUTEINIZING HORMONE (LH), which stimulates egg release in the ovaries and TESTOSTERONE secretion from the testes
- PROLACTIN, which stimulates milk production during BREASTFEEDING

These hormones all initiate hormonal cascades among other endocrine structures. Negative-feedback loops regulate the amounts of hormones the pituitary gland secretes, with secretions slowing or stopping when terminal hormones reach appropriate levels in the blood circulation. The hormones of the anterior pituitary are integral to the body’s STRESS RESPONSE HORMONAL CASCADE.

HORMONES OF THE ANTERIOR PITUITARY LOBE

ADRENOCORTICOTROPIN HORMONE (ACTH)	FOLLICLE-STIMULATING HORMONE (FSH)
LUTEINIZING HORMONE (LH)	GROWTH HORMONE (GH)
THYROID-STIMULATING HORMONE (TSH)	PROLACTIN

Posterior Lobe Structure and Hormones

The posterior lobe of the pituitary gland, also called the neurohypophysis, receives the hormones ANTIDIURETIC HORMONE (ADH) and OXYTOCIN from the hypothalamus and then stores them. The

posterior lobe does not itself synthesize any hormones. The hypothalamus regulates the posterior lobe primarily through neurologic signals (notably via the NEUROTRANSMITTER acetylcholine) that stimulate it to release its hormones into the blood circulation.

HORMONES OF THE POSTERIOR PITUITARY LOBE

ANTIIDIURETIC HORMONE (ADH)

OXYTOCIN

For further discussion of the pituitary gland within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also [ACROMEGALY](#); [ADENOMA](#); ANABOLIC STEROIDS AND STEROID PRECURSORS; CORTICOTROPIN-RELEASING HORMONE (CRH); GONADOTROPIN-RELEASING HORMONE (GNRH); GROWTH HORMONE-RELEASING HORMONE (GHRH); [HYPERPROLACTINEMIA](#); [HYPOPITUITARISM](#); THYROTROPIN-RELEASING HORMONE (TRH).

polyglandular deficiency syndrome An autoimmune disorder in which the IMMUNE SYSTEM produces antibodies that attack various endocrine glands and structures, resulting in deficiencies of the hormones the structures produce. The endocrine glands most commonly affected are the ADRENAL GLANDS, the THYROID GLAND, the PARATHYROID GLANDS, and the PITUITARY GLAND. When one autoimmune deficiency condition develops in an endocrine structure, others are likely to follow. The three types of polyglandular deficiency syndrome are

- type 1 polyglandular deficiency syndrome, which affects children under the age of 12 and typically affects the parathyroid glands, causing HYPOPARATHYROIDISM, and the adrenal glands, causing ADRENAL INSUFFICIENCY or ADDISON'S DISEASE
- type 2 polyglandular deficiency syndrome, which affects adults over the age of 30 and includes type 1 DIABETES, adrenal insufficiency or Addison's disease, and HYPOTHYROIDISM
- type 3 polyglandular deficiency syndrome, which affects women age 40 to 50 and includes THYROIDITIS, early MENOPAUSE, Addison's disease, and VITILIGO

Symptoms correlate to the endocrine glands affected and the endocrine disorders that result from damage to those glands. As well, symptoms may also affect functions such as FERTILITY, particularly when the thyroid gland is among the involved endocrine glands. Fertility requires a fairly precise endocrine balance throughout the body. The diagnostic path combines clinical evidence, history of symptoms, and laboratory tests that measure various HORMONE levels. All forms of polyglandular deficiency syndrome are chronic and require appropriate, lifelong HORMONE THERAPY to supplement or replace deficient hormones.

See also [ANTIBODY](#); [AUTOIMMUNE DISORDERS](#); [ENDOCRINE GLAND](#); [HYPERTHYROIDISM](#); [INSULIN RESISTANCE](#); [MULTIPLE ENDOCRINE NEOPLASIA \(MEN\)](#).

progesterone A steroid HORMONE the adrenal cortex of the ADRENAL GLANDS, the OVARIES, and the TESTES synthesize from a base of cholesterol. Adipose cells (fat cells) also synthesize small amounts of progesterone. Progesterone is a precursor hormone from which men and women synthesize TESTOSTERONE. The HYPOTHALAMUS initiates the hormonal cascade that results in progesterone synthesis with the release of GONADOTROPIN-RELEASING HORMONE (GNRH), which stimulates the anterior lobe of the PITUITARY GLAND to produce LUTEINIZING HORMONE (LH) and FOLLICLE-STIMULATING HORMONE (FSH). LH and FSH act on the gonads (sex glands), stimulating their hormone productions.

Women have significantly higher levels of progesterone, which vary cyclically with MENSTRUATION, than men. In women the primary role of progesterone is to prepare the UTERUS for PREGNANCY. Progesterone levels spike with OVULATION and remain elevated for about 10 days. If pregnancy occurs, the corpus luteum continues to secrete progesterone to maintain the uterine environment. Progesterone also stimulates growth of the mammary glands in the breasts. If pregnancy does not occur the corpus luteum deteriorates, ceases progesterone production, and MENSTRUATION begins. The primary role of progesterone in men is to testosterone production.

For further discussion of progesterone within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also [ANDROGENS](#); [BREAST HEALTH](#); [ESTROGENS](#).

prolactin A peptide HORMONE the anterior lobe of the PITUITARY GLAND synthesizes and secretes in response to the HYPOTHALAMUS's release of GONADOTROPIN-RELEASING HORMONE (GNRH). THYROID-RELEASING HORMONE (TRH) also stimulates prolactin production. Prolactin is biochemically similar to GROWTH HORMONE (GH). The primary function of prolactin is to stimulate BREAST development and milk production in women who are BREASTFEEDING. Prolactin also appears to play a role in certain immune responses. Other cells throughout the body also synthesize and secrete prolactin, which researchers believe is to enhance prolactin's immune functions. High levels of ESTROGENS in the

BLOOD, such as occur near the end of PREGNANCY, increase prolactin secretion. DOPAMINE, a peptide hormone the hypothalamus secretes, signals the pituitary gland to stop secreting prolactin. Pituitary ADENOMA (a noncancerous tumor) can cause excessive prolactin secretion, resulting in galactorrhea (abnormal milk production) in men as well as women.

For further discussion of prolactin within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ADRENOCORTICOTROPIN HORMONE (ACTH); ANTIDIURETIC HORMONE (ADH); [FOLLICLE-STIMULATING HORMONE \(FSH\)](#); [HYPERPROLACTINEMIA](#); [LUTEINIZING HORMONE \(LH\)](#); [OXYTOCIN](#).



relaxin A peptide HORMONE with poorly understood roles in reproduction and CHILDBIRTH. Relaxin receptors are widespread throughout the body in both men and women. In women the OVARIES, corpus luteum, and breasts—and the PLACENTA during PREGNANCY—produce relaxin. In men, the PROSTATE GLAND and the seminal vesicles produce relaxin. Relaxin is biochemically similar to INSULIN and has numerous effects on smooth MUSCLE tissue and collagen (connective tissue) in the UTERUS, reproductive tract, cardiovascular system, urinary system, and gastrointestinal system. During pregnancy relaxin facilitates collagen remodeling, the alterations that take place in the collagen structures of the ligaments and tendons that support the enlarging uterus. During CHILDBIRTH relaxin appears to, as the name implies, relax the smooth muscles of the CERVIX and uterus after contractions. In men relaxin may facilitate the transportation of SPERM through the seminal vesicles.

For further discussion of relaxin within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also [CHORIONIC GONADOTROPIN](#); ESTROGENS; OXYTOCIN; PROLACTIN; PROGESTERONE.

renin A peptide HORMONE the KIDNEYS produce that sets in motion the sequence of events to convert angiotensinogen, an inert enzyme the LIVER stores, to angiotensin II, a potent vasoconstrictor (chemical that causes the blood vessels to narrow and stiffen, which raises BLOOD PRESSURE). Angiotensin II also stimulates the adrenal cortex of the ADRENAL GLANDS to release ALDOSTERONE. The kidneys secrete renin whenever they sense a reduction in the fluid volume in the BLOOD that passes through them. Aldosterone causes the kid-

neys to increase the amount of sodium they withhold from the blood, which in turn draws more water back into the blood circulation. In combination, these actions increase blood volume and blood pressure. Aldosterone's presence in the blood circulation and its actions on the kidneys also suppress renin secretion. The sequence of events is the renin-angiotensin-aldosterone (RAA) system, the body's key mechanism for regulating blood pressure and blood volume.

The RAA balance adjusts nearly continuously, as the blood's pressure and volume fluctuate with body activities down to even the most minute metabolic alterations. The release of renin may surge when a person stands up, for example, and slow when a person lies down, and even when a person transitions from sleep to wake. The RAA system relies on the proper functioning of all three component elements; dysfunction of any results in HYPERTENSION (high blood pressure). Kidney disease, particularly RENAL FAILURE, and HYPERALDOSTERONISM are the most important health conditions that influence the RAA system because both interfere with the release of renin. The excessive aldosterone in the blood circulation with hyperaldosteronism suppresses renin release, and kidney disease may interfere with the ability of the kidneys to sense fluid volume or may damage the cells that synthesize renin.

For further discussion of renin within the context of the endocrine system's structure and function, please see the overview section "The Endocrine System."

See also [ANTIDIURETIC HORMONE \(ADH\)](#).

somatostatin A peptide HORMONE the delta cells of the ISLETS OF LANGERHANS in the PANCREAS primarily synthesize (produce). The HYPOTHALAMUS and

the gastrointestinal tract also synthesize somatostatin. Somatostatin is an inhibitory hormone that has numerous functions related to METABOLISM and growth. It stops the release of GROWTH HORMONE (GH), INSULIN, GLUCAGON, and the DIGESTIVE HORMONES. Somatostatin also slows the activity of the gastrointestinal tract by reducing the release of acids and enzymes necessary for digestion. These actions slow the rate with which the gastrointestinal tract absorbs NUTRIENTS. Somatostatin further blocks the LIVER from converting glycogen to GLUCOSE.

Endocrinologists use an injectable pharmaceutical somatostatin preparation, octreotide, to treat ACROMEGALY, a condition that results from excessive GH production. Like endogenous somatostatin, octreotide blocks the anterior lobe of the PITUITARY GLAND from secreting GH. Type 1 DIABETES, an autoimmune disorder that destroys islet cells, often reduces the ability of the islets of Langerhans to produce somatostatin. However, the numerous other sources within the body appear capable of maintaining an adequate supply.

For further discussion of somatostatin within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also AUTOIMMUNE DISORDERS; DIGESTIVE ENZYMES.

stress response hormonal cascade The hormonal responses that occur across endocrine structures to prepare the body to manage physiologic stress such as a strong increase in physical activity (for example, running). The stress response hormonal cascade begins when the HYPOTHALAMUS receives input that the body is experiencing stress. It releases a surge of CORTICOTROPIN-RELEASING HORMONE (CRH), which stimulates the anterior lobe of the PITUITARY GLAND

to produce ADRENOCORTICOTROPIN HORMONE (ACTH). Concurrently the hypothalamus releases THYROTROPIN-RELEASING HORMONE (TRH), which stimulates the anterior pituitary to produce THYROID-STIMULATING HORMONE (TSH). The hypothalamus further stimulates, through neurotransmitters, the adrenal medulla to increase the release of EPINEPHRINE and NOREPINEPHRINE. These hormones stimulate NERVE cell communication such as in the muscles.

ACTH instructs the adrenal cortex of the ADRENAL GLANDS to release CORTISOL, which has numerous effects on cardiovascular and pulmonary functions. Cortisol is the body's fight-or-flight HORMONE that increases BLOOD flow to critical organs, HEART RATE, BLOOD PRESSURE, and BREATHING rate. Cortisol also stimulates the LIVER to convert glycogen to GLUCOSE, ramping up the blood supply of this essential energy source. The increase in blood glucose causes the ISLETS OF LANGERHANS to release INSULIN, which prepares cells throughout the body to receive additional glucose. TSH directs the THYROID GLAND to increase secretion of the thyroid hormones to accelerate METABOLISM, increasing cellular use of the now-available glucose supplies.

This hormonal cascade remains in action for as long as the body needs the ability to respond to the physiologic stress it faces. For the example of running, this might be until the running stops and cardiovascular and pulmonary functions return to normal levels. When the stress passes the cascades gradually reverse until the body's hormone levels also return to normal. Fear, anger, and other intense emotions also can activate the stress response hormonal cascade. Persistent activation of the stress response hormonal cascade eventually becomes dysfunctional, with the potential to cause damage to blood vessels and organ systems.

See also ALDOSTERONE; HYPERTENSION; STRESS AND STRESS MANAGEMENT.

T

testosterone A steroid HORMONE the adrenal cortex of the ADRENAL GLANDS, the TESTES in men, and the OVARIES in women synthesize from a base ingredient of cholesterol. Adipose (fat) cells throughout the body also produce small amounts of testosterone. Testosterone is one of the ANDROGENS and the predominant male sex hormone. It is responsible for male secondary sex characteristics, male FERTILITY, and spermatogenesis (SPERM production). In men and women both testosterone is important for MUSCLE mass, BONE DENSITY, and LIBIDO (sex drive).

In men testosterone levels peak around age 22, then decline at the rate of about 10 percent per decade until about age 75. Changes in a man's body shape begin to take place when the testosterone level reaches about 60 percent of its peak level, when a man is in his late 50s and early 60s. These changes include diminishing muscle mass, increased and redistributed body fat, loss of the HAIR on the head, and slower sexual response. Some men equate these midlife changes with "male MENOPAUSE" or ANDROPAUSE. In women testosterone levels cyclically fluctuate with the MENSTRUATION until menopause, after which the levels of testosterone and ESTROGENS drop significantly. Some women experience diminished sexual response as a result.

Endocrinologists may prescribe low-DOSE testosterone supplement to restore sexual response in men and women. Testosterone supplement also enhances spermatogenesis in men and may be a treatment for male INFERTILITY.

For further discussion of testosterone within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ALOPECIA; ANABOLIC STEROIDS AND STEROID PRECURSORS; HIRSUTISM; HYPOGONADISM; INHIBIN; PROGESTERONE.

thymosin A peptide HORMONE the THYMUS produces that influences how and when T-cell lymphocytes (white BLOOD cells that fight INFECTION) mature. The epithelial cells of the outer structure of the thymus synthesize thymosin most actively during childhood. Researchers do not fully understand the functions of the thymus or thymosin, particularly in adulthood. Current research is exploring the potential for using thymosin supplement to treat diseases such as HEPATITIS C and HIV/AIDS.

For further discussion of thymosin within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also IMMUNODEFICIENCY; LYMPHOCYTE.

thyroid cancer Malignant growths that develop within the tissues of the THYROID GLAND. Thyroid CANCER may be primary (originating in the thyroid gland) or secondary (metastasizing from cancer that originates elsewhere in the body). Thyroid cancer is uncommon in the United States, with about 11,000 cases diagnosed each year, and occurs primarily in people who are over age 70. There are four kinds of thyroid cancer: papillary, follicular, medullary, and anaplastic.

Papillary thyroid cancer About 75 percent of people who have thyroid cancer have papillary CARCINOMA, which is highly curable when detected and removed while the tumor is still encapsulated and clearly defined. Papillary thyroid cancer generally begins as a painless, single lump (nodule)

arising from the follicular cells and tends to grow slowly. This form of thyroid cancer is more common in people who have had previous RADIATION THERAPY to the neck, lower face, or upper chest, and in people who have autoimmune (Hashimoto's) THYROIDITIS. When papillary thyroid cancer metastasizes, it does so through the lymphatic system and usually only to adjacent lymph nodes.

Follicular thyroid cancer About 15 percent of thyroid cancers are follicular carcinomas, which also develop in the follicular cells. Follicular carcinoma does not correlate to previous radiation therapy or benign thyroid conditions. This form of thyroid cancer tends to metastasize through the BLOOD circulation, causing secondary tumors remote from the original tumor. With early detection and treatment (before METASTASIS), follicular thyroid cancer is highly curable. After metastasis, however, the prognosis declines considerably.

Medullary thyroid cancer About 8 percent of thyroid cancers are medullary carcinomas, which develop in the parafollicular cells which synthesize CALCITONIN. Consequently, excessive blood levels of calcitonin in the absence of other health conditions strongly suggest this thyroid cancer. Because these cells are less organized structurally, cancer that arises from them is less clearly delineated and accordingly more difficult to see or feel. This form of thyroid cancer often occurs in the inherited genetic disorder MULTIPLE ENDOCRINE NEOPLASIA (MEN). Rarely, medullary thyroid cancer is inherited without MEN. Medullary thyroid cancer tends to metastasize early to adjacent lymph nodes. Distant metastasis to remote sites significantly worsens the prognosis.

Anaplastic thyroid cancer About 2 percent of people who develop thyroid cancer have anaplastic carcinoma, which is the most lethal of the cancers that involve the thyroid gland. It grows rapidly and spreads aggressively. Anaplastic thyroid cancer is more likely to develop in men over the age of 70 and is very rare in people under age 50.

Symptoms and Diagnostic Path

The typical symptom of any form of thyroid cancer is a painless lump or swelling in the neck. The person may see the swelling in the mirror or feel

the lump. Many times a doctor discovers a thyroid cancer during a routine medical examination or when examining the neck for other reasons. Some people experience difficulty swallowing or talking, depending on the location and size of the tumor.

The diagnostic path typically includes blood tests to measure the levels of the thyroid hormones, including THYROID-STIMULATING HORMONE (TSH), though the results may be normal. ULTRASOUND and a radioisotope iodine reuptake test can identify the tumor and provide some clues as to whether it is cancerous, though fine-needle aspiration (FNA) biopsy provides the definitive diagnosis. In FNA the endocrinologist uses a small needle and syringe to withdraw a sample of cells from the growth. Laboratory examination then determines whether the cells are cancerous, and what type of cancer is present.

Treatment Options and Outlook

For nearly all thyroid cancers, treatment is surgery to remove the thyroid gland (thyroidectomy) followed by radioactive iodine to kill any remaining thyroid cells. The radioactive iodine acts as a form of CHEMOTHERAPY and invades thyroid cells no matter where they are in the body. The exception is for medullary thyroid cancer, which arises from the parafollicular cells that do not take in iodine. The doctor may choose conventional chemotherapy or radiation therapy to follow surgery for medullary thyroid cancer. When a papillary thyroid cancer is small and contained, the doctor may feel lobectomy (removal of the involved lobe of the thyroid gland) is adequate. The decision must consider numerous factors, however, and the person who has thyroid cancer should make an informed choice based on full consideration of those factors.

Thyroid cancers detected and removed early in their development have the highest treatment success rate, and can be up to 90 percent curable (papillary and follicular). Medullary and anaplastic thyroid cancers are more difficult to diagnose in their early stages, and thus tend to be more advanced and often have metastasized by the time treatment begins. After thyroidectomy, it is necessary to take lifelong thyroid hormone supplements.

Risk Factors and Preventive Measures

The primary risk factor for papillary and anaplastic thyroid cancers is previous radiation therapy to the neck, lower face, or upper chest. Radiation exposure causes about 80 percent of papillary thyroid cancers. Family history may establish a risk for medullary thyroid cancer, as does having MEN. Risk factors for anaplastic thyroid cancer are unknown. Early diagnosis is the most effective measure for successful treatment.

See also [CANCER TREATMENT OPTIONS AND DECISIONS](#); [GOITER](#); [SURGERY BENEFIT AND RISK ASSESSMENT](#); [THYROID NODULE](#); [THYROID STORM](#).

thyroid gland An [ENDOCRINE GLAND](#) that spreads across the front of the [THROAT](#) somewhat in the shape of a butterfly. Reddish brown in color, the thyroid gland has two lobes that equally produce the hormones [CALCITONIN](#), [THYROXINE \(T₄\)](#), and [TRI-iodothyronine \(T₃\)](#), as well as a number of precursor (inactive) thyroid hormones. The cells responsible for thyroid hormone production are the thyroid epithelial cells, also called follicular cells, which appear in clusters called thyroid follicles. The follicular cells are the only cells in the body that take in iodine, a mineral essential for thyroid hormone formation. Interspersed among the thyroid follicles are the parafollicular cells, also called C cells, which synthesize calcitonin.

The Thyroid Hormones: Metabolic Regulation

About 90 percent of the thyroid gland's hormone production is T₄, so-called because its chemical structure contains four iodine molecules. The other 10 percent is primarily T₃ (a structure of three iodine molecules) along with a number of minor hormones with unknown functions in the body. Because the thyroid hormones are not water soluble, they leave the thyroid gland attached to protein carriers the [LIVER](#) produces called thyroid-binding globulin (TBG). The TBG transports the thyroid hormones through the [BLOOD](#) to cells throughout the body.

All cells have receptors for T₃ and T₄, as these thyroid hormones regulate cellular [METABOLISM](#) (the exchange of energy within the cell). The thyroid hormones are the only peptide hormones that can pass through the cell membrane to activate receptors within the cell cytoplasm. T₃ and T₄

appear to concentrate the enzymes that regulate the transfer of energy within cells. T₃ is about 10 times more potent than T₄, though about one tenth as abundant in the blood circulation. Researchers believe that after T₄ binds with cell receptors it drops an iodine molecule to transform into the more active T₃; however, they do not understand the precise mechanisms by which this takes place. T₃ that binds with cell receptors remains T₃.

On a larger scale the thyroid hormones regulate the body's metabolism as well, controlling how the body uses energy. The thyroid hormones regulate body temperature, lipid and carbohydrate metabolism, [HEART RATE](#), the force of the [HEART](#)'s contractions, and normal growth and development. Adequate thyroid hormone levels are also necessary for [FERTILITY](#) ([HYPOTHYROIDISM](#) is one of the most common causes of [INFERTILITY](#)) and for cognitive function.

Thyroid hormones are critical for normal [BRAIN](#) development in the unborn child as well as throughout childhood. Rarely a child is born without a thyroid gland or with a severely dysfunctional thyroid gland. This establishes congenital hypothyroidism, formerly called cretinism, a syndrome of pronounced growth and intellectual deficits. The damage is permanent without immediate [HORMONE THERAPY](#) to provide the body with the necessary thyroid hormones. Undetected fetal hypothyroidism results in permanent damage to the brain, [NERVOUS SYSTEM](#), and other organ systems and structures. Congenital hypothyroidism is rare in the United States because routine newborn and child health-care standards include regular screening for thyroid hormone levels.

Calcitonin: Bone Density and Calcium Balance

The parafollicular cells of the thyroid gland produce the peptide hormone calcitonin, which regulates the balance of calcium and phosphorus in the bones and blood. The thyroid gland releases calcitonin in response to elevated levels of calcium in the blood. Calcitonin binds with receptors in the [KIDNEYS](#), increasing the amount of phosphorus excreted into the [URINE](#), and in osteoblasts (cells within the bones that create new [BONE TISSUE](#)), stimulating them to accept calcium. Calcitonin functions in dynamic balance with [PARATHYROID](#)

HORMONE, which draws calcium from the bones into the blood to meet the calcium needs elsewhere in the body.

Generally, disorders of the thyroid gland have little effect on calcitonin synthesis because such disorders affect the follicular cells. A notable exception is an uncommon form of THYROID CANCER called medullary carcinoma, which develops in the parafollicular cells that synthesize calcitonin. Elevated levels of calcitonin in the blood circulation without corresponding parathyroid dysfunction raise the suspicion that such a cancer is present.

COMMON DISORDERS OF THE THYROID GLAND

GOITER	GRAVES'S DISEASE
HYPERTHYROIDISM	HYPOTHYROIDISM
POLYGLANDULAR DEFICIENCY SYNDROME	THYROID CANCER
THYROIDITIS	THYROID NODULE
THYROID STORM	

For further discussion of the thyroid gland within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also [AGING, ENDOCRINE CHANGES THAT OCCUR WITH](#); [HYPERCALCEMIA](#); [HYPERPARATHYROIDISM](#); [HYPOCALCEMIA](#); [HYPOPARATHYROIDISM](#).

thyroiditis INFLAMMATION of the follicular cells of the THYROID GLAND. The inflammation prevents these cells from synthesizing thyroid hormones, resulting in HYPOTHYROIDISM. In some forms of thyroiditis the inflammation resolves and the follicular tissue returns to normal thyroid HORMONE production. In other forms the inflammation heals but forms SCAR tissue (fibrosis), permanently destroying the ability of the affected follicular cells to synthesize thyroid hormones. Thyroiditis does not affect the parafollicular cells in the thyroid gland that produce CALCITONIN.

The three main types of thyroiditis are

- autoimmune thyroiditis, sometimes called Hashimoto's thyroiditis or chronic lymphocytic thyroiditis, which often develops in people who have other AUTOIMMUNE DISORDERS and is the most common type of thyroiditis
- silent thyroiditis, which often develops in women who have recently given birth and generally begins with HYPERTHYROIDISM
- subacute thyroiditis, also called granulomatous thyroiditis or subacute lymphocytic thyroiditis, which typically develops after a viral INFECTION

Other rare types of thyroiditis include Reidel's thyroiditis, in which the thyroid becomes fibrotic

THYROIDITIS SYMPTOMS AND TREATMENT

Autoimmune (Hashimoto's) Thyroiditis	Silent Thyroiditis	Subacute Thyroiditis
no PAIN	no pain	pain
gradual hypothyroid onset: progressive fatigue, weight gain, mild GOITER	hyperthyroid onset within four months of CHILDBIRTH: weight loss, anxiety, insomnia, agitation	rapid hyperthyroid onset: weight loss, anxiety, insomnia, agitation
permanent destruction of thyroid follicular cells	no treatment for HYPERTHYROIDISM because duration is short	transition to hypothyroid: weight gain, fatigue, lethargy
permanent HYPOTHYROIDISM with lifelong thyroid supplement HORMONE THERAPY	transition to hypothyroid eight months after childbirth: weight gain, fatigue, lethargy, DEPRESSION	swelling and tenderness of neck
	damage to thyroid follicular cells often permanent, with resulting permanent hypothyroidism	NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) may relieve pain and some INFLAMMATION
	lifelong thyroid supplement hormone therapy	THYROID GLAND often fully recovers and no treatment is necessary
		permanent hypothyroidism requires lifelong thyroid supplement hormone therapy

(scarred) and merges with surrounding structures, and acute thyroiditis, which is a serious and potentially life-threatening bacterial infection of the thyroid gland that requires emergency medical treatment.

Symptoms and Diagnostic Path

Sometimes the first indications of thyroiditis are the symptoms of hyperthyroidism, as the inflammation causes the follicular cells to release a surge of thyroid hormones into the BLOOD circulation. When the effect of this surge subsides thyroid hormone levels in the blood drop below normal, establishing a state of hypothyroidism. The diagnostic path begins with blood tests to measure thyroid hormone and ANTIBODY levels, and may include diagnostic imaging procedures such as ULTRASOUND or radioisotope iodine reuptake test to further evaluate thyroid function and the presence of any nodules or swelling.

Treatment Options and Outlook

When thyroid symptoms are transitory, as with silent thyroiditis and often with subacute thyroiditis, HORMONE THERAPY with thyroid supplement is not necessary. Nor is it necessary to treat the hyperthyroid phase, because this is typically of short duration. Lifelong thyroid supplement hormone therapy becomes necessary when scarring permanently destroys thyroid follicular cells.

Risk Factors and Preventive Measures

The primary risk for autoimmune thyroiditis is the existence of any other autoimmune disorders. Silent thyroiditis nearly always follows CHILDBIRTH, and subacute thyroiditis follows a viral infection. Knowing of these risks increases the chance of early diagnosis, which can minimize the course of the duration. However, there are no preventive measures for thyroiditis.

See also GRAVES'S DISEASE; THYROID CANCER; THYROID NODULE; THYROID STORM.

thyroid nodule A small growth that develops within the tissues of the THYROID GLAND. Most thyroid nodules (about 90 percent) are noncancerous. Thyroid nodules, like other thyroid disorders, are significantly more common in women than men and become increasingly common with

advancing age. Endocrinologists call a thyroid nodule "hot" when its tissue secretes thyroid hormones and "cold" when it does not. Most malignant (cancerous) thyroid nodules are cold, while nearly all hot nodules are benign (noncancerous).

Most thyroid nodules do not cause symptoms. The person may notice a lump on the front of the neck when looking in the mirror. Often the doctor detects a thyroid nodule during a ROUTINE MEDICAL EXAMINATION. Thyroid nodules may oversecrete thyroid hormones, resulting in symptoms of HYPERTHYROIDISM. The diagnostic path may include ULTRASOUND examination of the neck and a radioisotope iodine reuptake test, which measures the ability of the nodule to take in iodine. Normal thyroid tissue uses iodine to synthesize thyroid hormones. A nodule composed of tissue other than thyroid tissue (a cold nodule) does not take up iodine. A fine-needle aspiration (FNA) biopsy, in which the endocrinologist withdraws a small tissue sample from the nodule using a thin needle and a syringe, provides cells for laboratory examination to determine whether the nodule is cancerous. A single node is more suspicious than are multiple nodes.

Some thyroid nodules resolve on their own without treatment. The endocrinologist may prefer to surgically remove a thyroid nodule that is causing symptoms, including those of hyperthyroidism, or that is growing though often chooses a course of watchful waiting for asymptomatic nodules that biopsy negative for CANCER and are not growing. Thyroid nodules may occur in THYROIDITIS (INFLAMMATION of the thyroid gland) or HYPOTHYROIDISM (underactive thyroid gland).

See also AGING, ENDOCRINE CHANGES THAT OCCUR WITH; GOITER; THYROID CANCER.

thyroid-stimulating hormone (TSH) A peptide HORMONE the anterior lobe of the PITUITARY GLAND synthesizes in response to the HYPOTHALAMUS's production of THYROTROPIN-RELEASING HORMONE (TRH). TSH subsequently binds with TSH receptors on the follicular cells in the THYROID GLAND, stimulating them to synthesize the primary thyroid hormones TRIIODOTHYRONINE (T_3) and THYROXINE (T_4), as well as a number of minor or precursor hormones. TSH also influences the pituitary gland's secretion of PROLACTIN and GROWTH HORMONE (GH). TSH levels in

the blood may remain artificially high in HYPOTHYROIDISM, as the levels of thyroid hormones are chronically inadequate in this condition of underactive thyroid gland. TSH levels may be normal or low in HYPERTHYROIDISM (overactive thyroid gland), depending on the cause of the oversecretion of thyroid hormones.

For further discussion of TSH within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ADRENOCORTICOTROPIN HORMONE (ACTH); ANTIDIURETIC HORMONE (ADH); FOLLICLE-STIMULATING HORMONE (FSH); GROWTH HORMONE (GH); LUTEINIZING HORMONE (LH); OXYTOCIN; PARATHYROID GLANDS; PARATHYROID HORMONE.

thyroid storm A rare but life-threatening condition resulting from HYPERTHYROIDISM in which the body experiences an exaggerated response to the overproduction of thyroid hormones.

Thyroid storm is a medical emergency that requires rapid treatment.

Thyroid storm generates severe ARRHYTHMIA and tachycardia (disturbances of the HEART's electrical activity), high FEVER (disruption of the body's heat regulation mechanisms), congestive HEART FAILURE, significant electrolyte imbalances, and seizures or psychotic behaviors. Typically thyroid storm develops when a person who has undiagnosed hyperthyroidism, most commonly the result of GRAVES'S DISEASE, experiences physiologic stress such as INFECTION, trauma, or surgery. The circulating thyroid hormones overwhelm the cells, dramatically accelerating METABOLISM. The body's usual negative-feedback loop mechanisms fail, and the THYROID GLAND continues to pour thyroid hormones into the BLOOD circulation.

Symptoms and Diagnostic Path

The symptoms and signs of thyroid storm manifest rapidly and include

- severe NAUSEA, VOMITING, and DIARRHEA
- high fever (above 105°F)
- confusion and anxiety

- DYSPNEA (difficulty BREATHING) and TACHYPNEA (rapid breathing)
- racing or pounding PULSE (140 beats per minute or greater)

The diagnostic path begins with blood tests to measure the levels of thyroid hormones. Typically, THYROXINE (T₄) and TRIIODOTHYRONINE (T₃) are significantly elevated and THYROID-STIMULATING HORMONE (TSH) is low. However, the diagnosis is primarily clinical (based on signs and symptoms).

Treatment Options and Outlook

Treatment aims to bring thyroid hormone levels down as quickly as possible, usually with the medications methimazole or propylthiouracil (PTU). Follow-up administration of intravenous iodine blocks the thyroid gland from resuming thyroid hormone production. Plasmapheresis to filter thyroid hormones from the blood may be a treatment option for people who do not respond to these measures. Beta blocker medications such as propranolol help thwart the actions of thyroid hormones that reach cells throughout the body. Other therapies target symptoms, such as cooling to bring the body temperature down and medications to regulate the heart's rhythm. Once the person's status stabilizes, the endocrinologist typically begins treatment for the underlying hyperthyroidism, which may include surgery to remove the thyroid gland or radioactive iodine to destroy the thyroid gland's ability to produce thyroid hormones.

Without treatment, or when treatment begins too late, thyroid storm is fatal. With appropriate and timely treatment about 80 percent of people who experience thyroid storm survive. After treatment, lifelong HORMONE THERAPY with thyroid hormone supplement is necessary.

Risk Factors and Preventive Measures

The primary risk factor for thyroid storm is undiagnosed hyperthyroidism. Appropriate treatment for hyperthyroidism can eliminate the risk for thyroid storm.

See also HYPOTHYROIDISM; THYROIDITIS.

thyrotoxicosis See HYPERTHYROIDISM.

thyrotropin-releasing hormone (TRH) A peptide HORMONE the HYPOTHALAMUS produces in response to decreased levels of the thyroid hormones in the BLOOD circulation. TRH initiates the hormonal cascade that regulates the synthesis and release of thyroid hormones from the THYROID GLAND. TRH stimulates the anterior lobe of the PITUITARY GLAND to release THYROID-STIMULATING HORMONE (TSH). TSH in turn binds with TSH receptors on the surface of the follicular cells in the THYROID GLAND, stimulating them to produce TRIIODOTHYRONINE (T_3) and THYROXINE (T_4), the primary thyroid hormones. Increased levels of T_3 and T_4 in the blood circulation signal the hypothalamus to “turn off” TRH secretion.

For further discussion of TRH within the context of the endocrine system’s structure and function please see the overview section “The Endocrine System.”

See also [ANTIDIURETIC HORMONE \(ADH\)](#); [CORTICOTROPIN-RELEASING HORMONE \(CRH\)](#); [GONADOTROPIN-RELEASING HORMONE \(GNRH\)](#); [GROWTH HORMONE-RELEASING HORMONE \(GHRH\)](#).

thyroxine (T_4) A peptide HORMONE the THYROID GLAND synthesizes from iodine and the amino acid tyrosine, both of which enter the body from dietary sources. The follicular cells in the thyroid gland synthesize T_4 . Thyroxine is designated T_4 because its chemical structure contains four iodine molecules (as well as two tyrosine molecules). About 80 percent of the thyroid gland’s hormone production is T_4 . T_4 travels through the blood circulation bound to the protein carrier thyroxine-binding globulin (TBG), which the LIVER synthesizes. All cells in the body have receptors for T_4 , which passes across the cell membrane (cell wall) to bind with receptors in the cell cytoplasm. Upon binding T_4 appears to drop an iodine molecule to become the more potent TRIIODOTHYRONINE (T_3). In combination, T_3 and T_4 regulate cellular METABOLISM (the conversion of energy within cells).

The HYPOTHALAMUS regulates the thyroid hormone cascade, which it initiates by producing THYROTROPIN-RELEASING HORMONE (TRH). TRH stimulates the anterior lobe of the PITUITARY GLAND to secrete THYROID-STIMULATING HORMONE (TSH). TSH, in turn, stimulates the thyroid gland to synthesize and

release T_4 (as well as T_3). An underactive thyroid gland produces inadequate amounts of T_3 and T_4 , resulting in HYPOTHYROIDISM and slowed metabolism. An overactive thyroid gland produces too much T_3 and T_4 , resulting in HYPERTHYROIDISM and an accelerated metabolic rate. T_4 is the most common ingredient in thyroid hormone supplements.

For further discussion of T_4 within the context of the endocrine system’s structure and function please see the overview section “The Endocrine System.”

See also [THYROIDITIS](#); [THYROID STORM](#).

triiodothyronine (T_3) A peptide HORMONE the THYROID GLAND synthesizes from iodine and the amino acid tyrosine, both of which the body acquires through dietary sources. The follicular cells in the thyroid gland synthesize T_3 . Triiodothyronine is designated T_3 because its chemical structure contains three iodine molecules in addition to two tyrosine molecules. About 20 percent of the thyroid gland’s hormone production is T_3 . T_3 is about 10 times more potent than THYROXINE (T_4), the other major thyroid hormone. All cells in the body have receptors for T_3 , which passes across the cell membrane (cell wall) to bind with those receptors within the cell cytoplasm. T_3 then directly influences the cell’s DNA, guiding its production of proteins. In combination, T_3 and T_4 regulate cellular METABOLISM.

The HYPOTHALAMUS regulates the thyroid hormone cascade, which it initiates by producing THYROTROPIN-RELEASING HORMONE (TRH). TRH stimulates the anterior lobe of the PITUITARY GLAND to secrete THYROID-STIMULATING HORMONE (TSH). TSH, in turn, stimulates the thyroid gland to synthesize and release T_3 (as well as T_4). An underactive thyroid gland produces inadequate amounts of T_3 and T_4 , resulting in HYPOTHYROIDISM and slowed metabolism. An overactive thyroid gland produces too much T_3 and T_4 , resulting in HYPERTHYROIDISM and an accelerated metabolic rate. T_3 is sometimes an ingredient in thyroid hormone supplements.

For further discussion of T_3 within the context of the endocrine system’s structure and function please see the overview section “The Endocrine System.”

See also [THYROIDITIS](#); [THYROID STORM](#).



vasoactive intestinal peptide (VIP) See [DIGESTIVE HORMONES](#).

Wilson's disease A hereditary disorder in which the body does not properly metabolize copper, which allows deposits of copper to accumulate in various organs. Without treatment Wilson's disease is fatal; with treatment it is easily manageable.

Copper is an important mineral for the body's production of various enzymes, including those that facilitate HEMOGLOBIN synthesis. However, the body needs only a very small quantity of copper. In health the LIVER discharges excess copper, which enters the body through dietary sources, into the BILE. The bile carries the copper into the gastrointestinal tract for removal from the body in the feces. The KIDNEYS also extract some copper from the BLOOD circulation, passing it from the body in the URINE. In Wilson's disease a genetic MUTATION prevents the liver from discharging excess copper. Instead, it stores copper within its own tissues as well as sends it back out into the blood circulation. The blood deposits the copper in tissues throughout the body. As the copper accumulates, it causes scarring and other damage that interferes with the normal functions of the tissues.

Symptoms and Diagnostic Path

The symptoms of Wilson's disease vary according to the body system most severely affected, which is most often the liver or the BRAIN and SPINAL CORD. Liver involvement produces symptoms such as

- JAUNDICE (yellowish color to the SKIN)
- HEPATOMEGALY (enlarged liver) and SPLENOMEGALY (enlarged SPLEEN)
- ASCITES (fluid accumulation in the abdomen)

- NAUSEA and VOMITING
- abdominal discomfort or PAIN

Involvement of the brain, spinal cord, and other structures of the NERVOUS SYSTEM produces symptoms that may include

- difficulty moving the arms and legs
- tremors
- confusion
- difficulty speaking and swallowing
- cognitive and memory dysfunction

A conclusive clinical sign for Wilson's disease is the appearance of a copper-colored ring around the iris of the EYE, called a Kayser-Fleischer ring. Other diagnostic indications include low levels of copper in the blood and high levels of copper in the urine. Biopsy of the liver or the kidneys shows the copper deposits in the tissues.

Treatment Options and Outlook

Treatment targets blocking the body's absorption of copper as well as removal of excessive copper already in the body (chelation). Commonly used chelation agents include penicillamine and trientine. These drugs bind with the copper, allowing the kidneys to excrete the bound molecules from the body in the urine. Zinc acetate can help reduce gastrointestinal absorption of copper from the diet. Doctors recommend eating foods that are low in copper. People who have Wilson's disease should drink bottled water because copper is common in household plumbing and should avoid cooking with copper pans or implements. The endocrinologist may also recommend a zinc supplement, as zinc interferes with copper absorption.

FOODS HIGH IN COPPER

avocado
chocolate
dried fruits: apricots, figs, nectarines, raisins
energy bars and drinks
legumes: black beans, garbanzo beans, kidney beans, lentils,
navy beans, pinto beans, peanuts, soybeans, split peas
mushrooms
nuts: almonds, cashews, hazelnuts, macadamia, pecans,
walnuts
organ meats: gizzard, heart, liver, kidney
shellfish: clams, mussels, oysters, scallops, shrimp
whole grains: barley, bran

Risk Factors and Preventive Measures

Wilson’s disease occurs as a result of autosomal recessive GENE mutation. People with a family history of Wilson’s disease can undergo GENETIC TESTING for this mutation. Minimizing copper intake prevents excessive accumulation and its resultant damage and symptoms. Damage that has already occurred at the time of diagnosis is often permanent.

See also COGNITIVE FUNCTION AND DYSFUNCTION; GENETIC DISORDERS; HEMATOCHROMATOSIS; INHERITANCE PATTERNS; MEMORY AND MEMORY IMPAIRMENT; PHENYLKETONURIA (PKU).

THE URINARY SYSTEM

The urinary system cleanses metabolic wastes and toxins from the blood. Physician specialists who treat conditions of the urinary system are urologists (surgeons) and nephrologists (internists). This section, "The Urinary System," presents a discussion of the organs and structures of the urinary system, an overview of urinary and renal health and disorders, and entries about the health conditions that involve the urinary system.

Structures of the Urinary System

KIDNEYS	NEPHRON
cortex	ureters
medulla	BLADDER
renal pelvis	URETHRA

Functions of the Urinary System

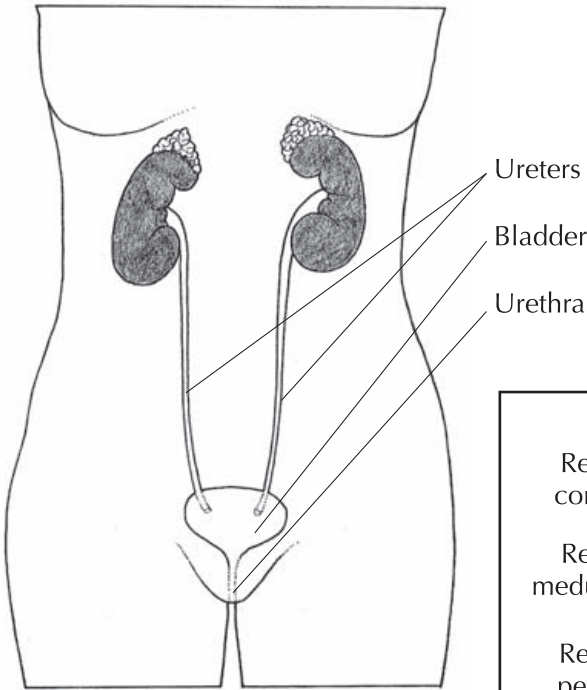
The primary functions of the urinary system's organs and structures are to filter and excrete wastes from the BLOOD and to maintain the body's fluid and electrolyte balances. The KIDNEYS make, and the bladder contains and then excretes, urine, a watery fluid that carries dissolved and suspended wastes from the body. As well, the KIDNEYS produce two essential hormones: RENIN, which helps regulate BLOOD PRESSURE, and ERYTHROPOIETIN (EPO), which stimulates the BONE MARROW to produce erythrocytes (red blood cells). The kidneys also convert vitamin D from its inactive dietary form to its active form as the HORMONE calcitriol, which is necessary for proper calcium absorption.

The kidneys: cleansing the blood The paired KIDNEYS reside in the upper posterior abdomen, behind the peritoneum along the spine and within the protection of the rib cage. The kidneys are slightly offset from one another in the symmetry of their positioning, with the right kidney being about an inch lower than the left to accommodate the LIVER. Each kidney is about the size of a man's fist, shaped like the bean that bears its name. The dark reddish brown kidneys curve toward each other, turning their backs to the

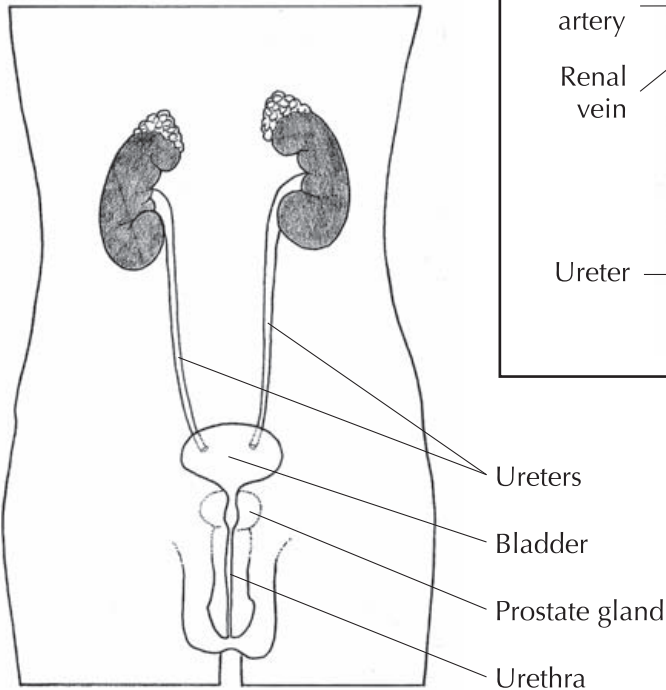
body's sides. Though the kidneys have a combined weight of about 10 ounces, they hold 20 percent of the body's blood supply. The renal arteries branch directly from the abdominal AORTA, ensuring that the kidneys are among the first of the organs to receive blood with each contraction of the HEART. The renal veins channel blood returning to the circulation from the kidneys directly to the inferior VENA CAVA.

The kidney's structure features two general divisions. The outer layer is the renal cortex, intensely vascular tissue where the filtration of blood takes place. The inner layer is the renal medulla, where URINE collects. The workhorse structure of the kidney is the microscopic NEPHRON, which is made up of two elements: the renal corpuscle, contained in the renal cortex, and the tubule, contained in the renal medulla. The renal corpuscle consists of a containment capsule (called Bowman's capsule) that encloses the GLOMERULUS, a tightly coiled capillary network that receives blood from the body for filtration. The space between the inner wall of Bowman's capsule and the walls of the glomerulus collects the molecules of water, electrolytes, and metabolic wastes that pass from the blood, forming a mixture called the filtrate. The tubule is a loosely coiled structure that wraps around the renal corpuscle. It reabsorbs electrolytes and water the body needs from the filtrate and sends the remainder on with the wastes to become urine. Each tubule is about 1.25 inches in total length; were a kidney's tubules removed and stretched

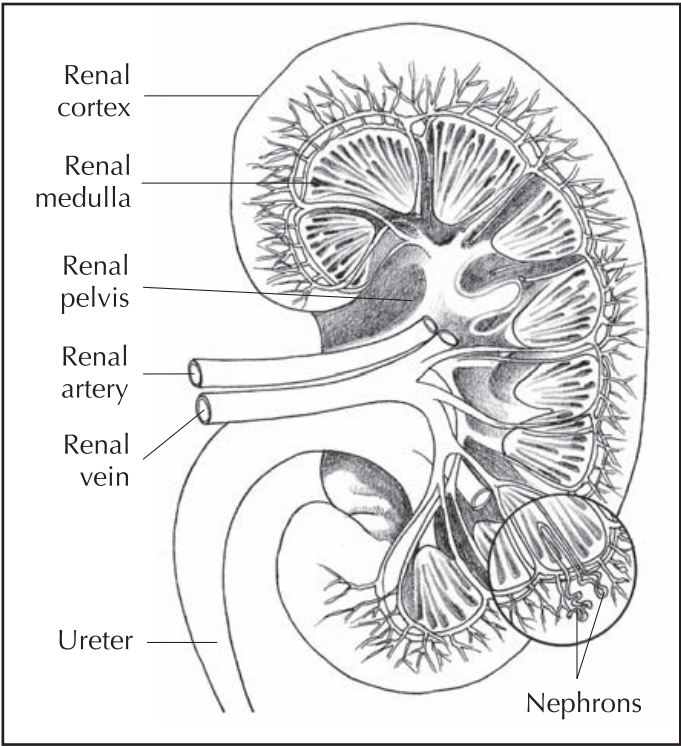
The Urinary System



Female



Male



Kidney

end to end in a straight line, they would cover more than 50 miles.

**RENAL DIALYSIS: MACHINES TO CLEANSE
THE BODY WHEN THE KIDNEYS CANNOT**

Researchers began working in the 1920s to develop a safe, effective substitute to cleanse metabolic wastes from the BLOOD when the KIDNEYS failed. By the early 1950s such a substitute—the hemodialysis machine—entered clinical use. And by the 1970s hemodialysis was the standard treatment for END-STAGE RENAL DISEASE (ESRD). Today nearly 300,000 Americans rely on hemodialysis.

The kidneys and blood pressure The kidneys regulate blood pressure by controlling the volume of the blood and through the production of the hormone renin, which is the cornerstone of the body's RENIN-ALDOSTERONE-angiotensin (RAA) system for regulating blood pressure. Renin and aldosterone initiate chemical actions that result in constricting blood vessels and increasing blood volume to raise blood pressure.

The tubules in the nephrons continuously adjust the amounts of sodium, potassium, and chloride they reabsorb from the filtrate. Where goes the electrolytes, so goes the water. The more of electrolytes the tubules draw back into the blood, the higher the amount of water that follows. Increased reabsorption increases blood volume and raises blood pressure. Decreased reabsorption sends the electrolytes in the filtrate, along with the water that they draw, out of the body in the urine to drop both blood volume and blood pressure.

Within each nephron, where the distal tubule and the afferent arteriole (the blood vessel that brings blood into the glomerulus) nearly touch, are two clusters of specialized sensory cells. The macula densa resides within the walls of the distal tubule; its cells sense the concentration of electrolytes, primarily sodium, in the filtrate. In the interstitial space between the distal tubule and the afferent arteriole are the juxtaglomerular cells, which sense the pressure of the blood as it courses through the afferent arteriole.

The clusters are in constant communication with one another, using chemical signals to regu-

late how much electrolytes and water the tubules reabsorb from the filtrate. As well, these cell clusters send a continuous barrage of NERVE signals to the brainstem, which just as continuously determines the adjustments in renin release necessary to maintain the blood pressure at the level the body needs. Renin sets in motion the cascade of chemical events that converts the inactive protein angiotensinogen (also called angiotensin I) into the very potent vasoconstrictor (chemical that causes the blood vessels to narrow and stiffen, raising blood pressure) angiotensin II. Angiotensin I causes the peripheral arterioles to constrict.

Angiotensin II also signals the adrenal cortex of the ADRENAL GLANDS to release ALDOSTERONE, a hormone that stimulates the tubule to pull even more sodium (and, of course, water) back into the blood from the filtrate. The result is a rise in blood pressure. The brainstem also instructs the HYPOTHALAMUS to release ANTIDIURETIC HORMONE (ADH) when blood volume and pressure fall below a certain threshold and to withhold ADH when blood volume is above that threshold. The threshold varies with the body's activities, and the cascade of actions is a process of perpetual adjustment.

Doctors take advantage of these mechanisms to treat HYPERTENSION (high blood pressure). Diuretic medications—"water pills"—act on the tubules to block them from reabsorbing sodium and chloride. This increases the amount of water in the filtrate, preventing the tubules from increasing blood volume. Various antihypertensive medications, such as angiotensin-converting enzyme (ACE) inhibitors, target different stages of the angiotensin conversion process.

The kidneys and fluid balance The processes of the kidney that regulate blood pressure also maintain the body's fluid and electrolyte balances. The hypothalamus monitors the amount of water in the body, using ADH as the chemical messenger that tells the kidneys the body needs more water or less water.

The kidneys and erythropoiesis It seems a bit odd, at first, that the kidneys produce the hormone that stimulates the bone marrow to produce new erythrocytes (red blood cells). But no other organs have such intimate exposure to the blood that they can literally "examine" each cell. With every heartbeat 20 percent of the body's blood

volume surges through the kidneys. This blood disperses among the million or so glomeruli, the microscopic capillaries within the nephrons. Specialized sensors in the walls of the glomeruli detect the levels of oxygen in the erythrocytes as they pass by. Low levels of oxygen stimulate the kidneys to synthesize (produce and release) EPO. EPO travels through the blood circulation to the bone marrow, where it stimulates the production of new erythrocytes (erythropoiesis).

Erythropoiesis suffers in RENAL FAILURE because the blood cannot circulate through the glomeruli, resulting in ANEMIA. This is why people who have renal failure feel so fatigued. And erythropoiesis comes to a near-halt in ESRD, when the kidneys no longer function at all. Not only do toxins accumulate in the blood when the kidneys fail but also the blood cannot deliver enough oxygen because it does have enough red blood cells to carry the load. Many people who have renal failure take EPO supplement, a product of RECOMBINANT DNA technology, to maintain adequate erythropoiesis.

The kidneys and bone health Mention *strong bones* and the first association is likely to be “calcium.” It might just as well be calcitriol, the hormone form of vitamin D, because without calcitriol, the body cannot use the calcium it receives. The kidneys convert dietary vitamin D, a fat-soluble vitamin inert within the body in its dietary form, to calcitriol. The kidneys further participate in the body’s calcium balance because they determine how much calcium to reabsorb from the filtrate and return to the blood circulation.

Calcium is essential for numerous body activities ranging from HEALING and cell repair to nerve and MUSCLE cell communication. Calcium makes it possible to walk across the room, from the SKELETON that supports the body to the nerve impulses that instruct muscle fibers from heart to soles to contract. People who have chronic renal failure and other forms of chronic renal disease often take vitamin D supplement (calciferol). Adequate vitamin D is essential for appropriate growth in children; without it there is no growth. PARATHYROID HORMONE ACTS on the distal tubule to increase the amount of calcium the tubule reabsorbs.

The kidneys and urine production This most familiar and seemingly simple function of the kidneys is, of course, its most important. Without the

urine to carry metabolic wastes from the blood, none of the kidney’s other functions would be necessary for very long. Urine is a mixture of the water, electrolytes, and metabolic wastes (primarily urea) the kidneys extract from the blood. As blood passes through the glomerulus pressure squeezes much of the blood’s water, along with electrolytes and wastes, through the glomerular walls into Bowman’s capsule. This mixture, the filtrate, collects in the capsule and drains into the tubule. The tubule reabsorbs about two thirds of the water and electrolytes, passing on the remainder to become urine. Collecting tubules carry the urine into the renal pelvis, where it drains into the ureters that then channel it to the BLADDER.

Holding the urine: the bladder Suspended in the lower pelvis is the bladder, an expandable muscular sac that collects the urine that drains from the kidneys. When empty the bladder is about the size of a lemon; when filled to its capacity of about 500 milliliters the bladder is about the size of a cantaloupe. Its three-layer wall consists of a mucous inner layer, middle layer of smooth muscle, and fibrous membrane outer layer. The middle layer, called the detrusor muscle, relaxes to allow the bladder to distend when filling with urine and contracts to push urine from the bladder into the URETHRA for passage from the body.

The bladder holds the urine in a more colloquial sense as well, allowing conscious override of the micturition REFLEX, an involuntary function of the sympathetic NERVOUS SYSTEM, that initiates URINATION. At about two or three years of age the brain, muscles, and nerves have matured enough for conscious control to take over certain involuntary functions. Voluntary urination—toilet training—is the hallmark of this effort and marks the rite of passage from baby to child. Voluntary control of urination uses certain centers in the brain in coordination with voluntary muscles such as the pubococcygeal muscle to manage the timing of urination, though if the bladder becomes too full the micturition reflex becomes too intense for conscious control to overcome.

Tubes of urine transport: the ureters and urethra From each kidney a thin muscular tube drops about 12 inches to join with the bladder. Urine trickles from the kidney’s collecting tubules into the renal pelvis, a deltalike structure that

channels the urine toward the URETER, which will carry the urine, like a drain, into the bladder. Though small in diameter the ureter has relatively thick, sturdy walls that contract in rhythmic waves to move urine in a steady flow. The ureter's peristaltic action also helps prevent urine from flowing back up into the kidney. Each ureter inserts into the back of the bladder wall, tunneling through the detrusor muscle for a short distance before emerging into the urothelium (inner epithelial layer of the bladder). The tunnel is another safeguard to keep urine from backflowing to the kidney, flattening unless pressure from flowing urine causes it to open.

The urethra carries urine from the base of the bladder to outside the body. A woman's urethra is less than two inches long and exits her body between the CLITORIS and the VAGINA. A man's urethra is about eight inches long and exits his body at the tip of the PENIS. A ring of muscle, the urethral sphincter, encircles the urethra at the neck of the bladder. When contracted the sphincter holds the urethra closed and urine remains in the bladder; when relaxed the sphincter allows the urethra to open and urine to leave the bladder.

Health and Disorders of the Urinary System

The kidneys have remarkable capacity. Each kidney contains more than a million nephrons. Though the normal design of the human body features two kidneys, one healthy kidney is perfectly able to meet the needs of the body. The kidneys can lose as much as 65 to 70 percent of their ability to function and still maintain the health of the body. When kidney function reaches 25 percent, however, the filtration workload overwhelms the nephrons and symptoms of kidney failure begin to manifest. And when kidney function drops to 15 percent or lower, the kidneys can no longer perform at a level that sustains life.

The most significant health challenges that confront the kidneys are DIABETES and hypertension, which are especially dangerous when they occur in combination as they do in about half of people who have diabetes as hypertension is a complication of diabetes. These two conditions place inordinate stress on the glomeruli, hypertension because it increases the pressure under which blood enters the glomeruli and diabetes because

the elevated levels of GLUCOSE in the blood damage capillaries throughout the body. The glomeruli, being among the most intensely concentrated capillary networks in the body, bear the brunt of such damage. About 20 million Americans live with some degree of kidney failure and another 10 million are at risk of kidney failure because of health conditions such as diabetes and hypertension as well as conditions that directly affect the kidneys.

HEALTH CONDITIONS THAT AFFECT
THE URINARY SYSTEM

ALPORT'S SYNDROME	BLADDER CANCER
BLADDER EXSTROPHY	CYSTINURIA
CYSTITIS	CYSTOCELE
END-STAGE RENAL DISEASE (ESRD)	EPISPADIAS
FANCONI'S SYNDROME	GLOMERULONEPHRITIS
GLOMERULOSCLEROSIS	GOODPASTURE'S SYNDROME
HEMOLYTIC UREMIC SYNDROME	HEPATORENAL FAILURE
HORSESHOE KIDNEY	HYDRONEPHROSIS
HYPOSPADIAS	NEPHRITIS
NEPHROLITHIASIS	NEPHROPATHY
NEPHROTIC SYNDROME	POLYCYSTIC KIDNEY DISEASE
RENAL CANCER	RENAL CYST
RENAL FAILURE	RENAL TUBULAR ACIDOSIS
UREMIA	URETHRAL STRICTURE
URETHRITIS	URINARY INCONTINENCE
URINARY TRACT INFECTION (UTI)	UROLITHIASIS
VESICOURETERAL REFLUX	WILMS'S TUMOR

Traditions in Medical History

Among the earliest known medical treatments are those for kidney stones and bladder stones. Ancient healers across cultures documented various remedies, including surgical removal, for the painful conditions known today as NEPHROLITHIASIS and UROLITHIASIS, respectively. Though early physicians could not examine the urinary structures themselves in any great detail, these structures abundantly produced a substance that many physicians turned into a diagnostic oracle: the urine. The gifted physician was one who could study the color, cloudiness, consistency, odor, and even taste of the urine to diagnose conditions ranging from HEART FAILURE to PREGNANCY to SYPHILIS and, of course, diabetes. This was the practice of uroscopy, the forerunner of modern urinalysis.

Greek philosopher and scientist Aristotle (384–322 B.C.E.), whose father was a physician,

described the urinary system's basic structure and function in his writings. However, nearly 2000 years would pass before one of science's most significant inventions, the light microscope, would give 17th-century scientists the opportunity to explore the amazing structure and function of the kidney beyond the human EYE's ability to detect. Advances in modern times such as the electron microscope, which debuted in the 1950s, and the mapping of the human GENOME, completed in 2003 after 13 years of research, extended to the molecular level understanding of the seemingly simple yet incredibly intricate mechanisms that filter the blood and cleanse the body of metabolic wastes.

Breakthrough Research and Treatment Advances

The first successful KIDNEY TRANSPLANTATION in 1954, in which surgeons removed one healthy kidney from a man and transplanted it into his identical twin brother whose kidneys had completely failed, marked the advent of a new era in

modern medicine. The discovery of cyclosporine, a powerful immunosuppressive DRUG, in 1954, made kidney transplantation a viable treatment for ESRD and paved the way for the transplantation of other vital organs such as livers and hearts. Today, surgeons in the United States perform more than 15,000 kidney transplantations each year, making the kidney the most frequently transplanted organ (aside from SKIN and corneas). Yet 45,000 people wait for donor kidneys. The shortage of donor kidneys has spurred efforts to find new solutions. One direction of research focuses on living kidney donation, in which a person agrees to provide one of his or her kidneys to a person whose own kidneys have failed. Advances in MINIMALLY INVASIVE SURGERY have significantly reduced the risks and inconveniences for living donors. Other directions of research focus on molecular medicine and genetics, looking for ways to correct problems with the kidneys to prevent kidney failure.

aging, urinary system changes that occur with

At birth the structures of the urinary system are fully developed and function under the automatic control of the NERVOUS SYSTEM. The newborn's KIDNEYS filter BLOOD and make URINE. The BLADDER collects the urine and, when it fills to a point that triggers the micturition REFLEX, it empties to drain urine via the URETHRA to outside the body. Voluntary control over URINATION develops between three and five years of age, the rite of passage from babyhood to childhood. The urinary system typically then functions at a steady level for decades, unless disease alters its structures (notably the KIDNEYS).

Changes in the Kidneys and Bladder

Beginning around age 40 the number, size, and efficiency of nephrons, the filtering units of the kidneys, begins to diminish. At birth each kidney contains a million or more nephrons. By age 70 the kidneys have lost about 30 percent of the nephrons they contained at birth. They are smaller overall in size and take longer to filter the blood that flows through them. They may allow more water to enter the urine and keep more electrolytes in the blood circulation. The imbalance, even when slight, often affects BLOOD PRESSURE and other vital functions and increases the risk for DEHYDRATION.

Other changes in the body often affect the kidneys as well as other structures of the urinary system. With aging fibrous tissue throughout the body begins to lose elasticity, becoming more rigid. This reduced FLEXIBILITY can harden and narrow the blood vessels that supply the kidneys, slowing blood flow into the kidneys and through the nephrons. It also diminishes the bladder's ability to distend (expand), decreasing bladder capacity.

Age-related changes in NERVE and BRAIN function also slow the micturition REFLEX, allowing the bladder to become more full before triggering the urge to urinate. These changes can result in URINARY URGENCY and URINARY FREQUENCY.

The Effects of Other Changes and Health Conditions

Age-related changes in the reproductive system—MENOPAUSE in women and BENIGN PROSTATIC HYPERPLASIA (BPH) in men—affect the urinary system as well. The normal and usually harmless enlargement with aging of the PROSTATE GLAND in men can constrict the urethra, interfering with the flow of urine during urination. Relaxation of the pelvic structures that accompanies the decline of the levels of ESTROGENS in women who are past menopause affects the woman's ability to control the flow of urine, allowing problems such as stress incontinence (urine leakage with coughing, sneezing, or laughing). As well, stretching and tearing of the pelvic muscles and ligaments that may have occurred during PREGNANCY and CHILDBIRTH may weaken these structures, allowing the bladder to sag and pressure the VAGINA (CYSTOCELE).

HYPERTENSION (high blood pressure) and DIABETES, two conditions that become increasingly common with advancing age, are particularly hazardous to the kidneys and between them account for about 80 percent of RENAL FAILURE (acute and chronic) and END-STAGE RENAL DISEASE (ESRD). Early and appropriate treatment for these conditions can significantly slow their actions on the kidneys, highlighting the importance of routine health screening for them. The risks for BLADDER CANCER, RENAL CANCER, NEPHROPATHY, NEPHROLITHIASIS (kidney stones), and UROLITHIASIS (bladder stones) also increase with age.

Measures to Maintain Urinary Health

Though it is not possible to prevent many of the health conditions affecting the urinary system that become more common with age, there are preventive lifestyle measures that can help maintain urinary health. These include

- drink a minimum of 8 to 12 eight-ounce glasses of water daily, more when it is hot or with exercise (urine should be colorless or slightly yellow)
- get blood pressure checked by a health-care provider at least yearly
- get checked for diabetes regularly
- urinate when the urge occurs and empty the bladder completely when urinating
- minimize use of over-the-counter products containing acetaminophen or NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)
- do not smoke (cigarette smoking accounts for 50 percent of bladder cancers)

Maintaining a healthy weight, nutritious EATING HABITS, and daily physical exercise are important for good health overall. People who have diagnosed hypertension or diabetes should strive to maintain the best possible control over these conditions through appropriate lifestyle measures and by taking medications as prescribed.

See also [ATHEROSCLEROSIS](#); [HEPATORENAL FAILURE](#); [LIFESTYLE AND HEALTH](#); [URINARY INCONTINENCE](#).

albuminuria Excessive excretion of ALBUMIN, a form of protein, into the URINE. Albuminuria, also called proteinuria, typically indicates kidney conditions that affect the glomeruli (the tubular structures within the KIDNEYS that filter wastes and excess water from the BLOOD to excrete in the urine). Such conditions include GLOMERULONEPHRITIS, GLOMERULOSCLEROSIS, NEPHROTIC SYNDROME, and NEPHROPATHY of DIABETES or of HYPERTENSION (high BLOOD PRESSURE). Albuminuria may accompany cardiovascular diseases such as ENDOCARDITIS and chronic inflammatory diseases such as SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) and RHEUMATOID ARTHRITIS. Strenuous physical exercise also can cause transient albuminuria without kidney disease.

Albuminuria does not itself cause symptoms. Most often the doctor detects albuminuria through urinalysis done during a ROUTINE MEDICAL EXAMINATION. Treatment targets the underlying cause. In the circumstance of chronic kidney disease, monitoring the urine albumin level is one method for assessing the status of kidney function. The urologist may conduct further diagnostic procedures such as ULTRASOUND or kidney biopsy when the cause of the albuminuria is undetermined. Persistent albuminuria typically suggests progressive damage to the kidneys regardless of the underlying cause.

See also [AMYLOIDOSIS](#); [MINIMAL CHANGE DISEASE](#).

Alport's syndrome An inherited genetic disorder in which one, two, or three mutations occur in the GENE that encodes type IV collagen formations, also called basement membranes. The mutations affect up to three of the six protein chains (alpha-3, alpha-4, and alpha-5) that make up type IV collagen, which is a foundation for a number of structures in the body including the glomeruli in the KIDNEYS, COCHLEA in the inner EAR, LENS of the EYE, and alveoli in the LUNGS. Among the three variations of Alport's syndrome, two include damage to these other structures as well as to the kidneys. All variations of Alport's syndrome include kidney damage that manifests as chronic GLOMERULONEPHRITIS (INFLAMMATION of the glomeruli), resulting in progressive scarring and fibrosis of the glomeruli. The fibrotic tissue replaces healthy tissue, preventing normal glomerular function.

The most common inheritance pattern for Alport's syndrome is X-linked, which affects about 80 percent of those who have the disorder. The syndrome may also occur as an autosomal recessive pattern (15 percent) or an autosomal dominant pattern (5 percent). All types of Alport's syndrome eventually progress to END-STAGE RENAL DISEASE (ESRD) in nearly everyone who has the disorder, though the rate of progression is highly variable and differs among the three inheritance patterns for the syndrome.

Symptoms and Diagnostic Path

The most common symptom of Alport's syndrome is HEMATURIA (bloody URINE) that may appear in

early childhood, typically following an upper respiratory viral INFECTION such as a cold. As the damage to the kidneys progresses, symptoms expand to include ALBUMINURIA (excessive albumin or protein in the urine) and HYPERTENSION (high BLOOD PRESSURE). About 80 percent of those who have Alport's syndrome develop neurosensory HEARING LOSS by ADOLESCENCE, and 15 percent have irregularities in the shape of the lens of the eye (lenticonus).

Symptoms in combination with family history strongly suggest Alport's syndrome, though kidney biopsy is the definitive diagnostic tool. Kidney biopsy, in which the urologist extracts a core of kidney tissue using a large-gauge needle, allows the him or her to determine the absence of any of the three affected protein chains as well as to assess the degree of damage already present. SKIN biopsy can confirm X-linked Alport's syndrome because the skin in this type of the disorder lacks the alpha-5 protein chain.

Treatment Options and Outlook

Treatment is primarily supportive and targets symptoms such as hypertension, hearing loss, and VISION IMPAIRMENT. For people who reach ESRD, KIDNEY TRANSPLANTATION often offers a viable therapeutic course. With treatment, many people who have Alport's syndrome are able to enjoy the

lifestyles of their choosing well into the fifth or sixth decade of life. The likelihood of RENAL FAILURE increases with age, however.

Risk Factors and Preventive Measures

Because Alport's syndrome is an inherited genetic disorder, the only risks for this condition are the causative gene mutations. There are no measures to prevent the condition. Early treatment for consequential health conditions and close medical monitoring of kidney function help maintain optimal health.

See also ALVEOLUS; GENETIC DISORDERS; GLOMERULUS; INHERITANCE PATTERNS; MUTATION; [RENAL DIALYSIS](#).

anuria The failure to produce URINE. Numerous circumstances can result in anuria, from severe DEHYDRATION and severe HYPOTENSION (low BLOOD PRESSURE) to END-STAGE RENAL DISEASE (ESRD) and RENAL FAILURE. Anuria requires prompt medical evaluation to determine and remedy the underlying cause. Without such correction, waste byproducts accumulate to toxic levels and the body cannot continue to function.

See also [DYSURIA](#); [ENURESIS](#); [NOCTURIA](#); [OLIGURIA](#); [URINARY INCONTINENCE](#).

azotemia See [UREMIA](#).

B

bladder A muscular, saclike structure in the lower pelvis that serves as a reservoir for the URINE the KIDNEYS produce. In women the bladder is in front of and slightly below the UTERUS. During PREGNANCY the expanding uterus limits the bladder's ability to expand, accounting for the URINARY FREQUENCY common in pregnancy's last trimester. In men the bladder is in front of the RECTUM, with the PROSTATE GLAND encircling the first segment of the URETHRA as it exits the bladder. Swelling of the prostate gland, such as typically occurs with advancing age, as in BENIGN PROSTATIC HYPERPLASIA (BPH), can constrict the flow of urine through the urethra in a man, accounting for symptoms such as urinary frequency and dribbling.

Three layers of tissue form the bladder. The outermost and innermost layers are membranous, the outer being a continuation of the peritoneum that lines the abdominal cavity and the inner being mucous-secreting epithelium. The bladder's middle layer is smooth MUSCLE called the detrusor muscle that itself has three layers, the fibers of each running differently. The outer muscle fibers run longitudinally (lengthwise), the middle muscle fibers form patterns of circles that ultimately culminate in the sphincter muscle that encloses the bladder's neck, and the inner muscle fibers run laterally (crosswise). Together these muscle layers allow the bladder to expand to accommodate the urine draining from the kidneys and also to contract, in coordination with relaxation of the urethral sphincter, to expel urine from the bladder through the urethra.

The ureters drain urine from the kidneys into the bladder; the urethra drains urine from the bladder to the outside of the body. One URETER, a narrow tubelike structure, drops from each kidney and enters the back wall of the bladder near its

midline. Urine drips continuously from the ureters into the bladder. The urethra, a somewhat muscular tube, carries urine from the bladder to outside the body. When empty the bladder is about the size of a large lemon; when filled to its capacity of about 500 milliliters (32 to 34 ounces) the bladder can reach the size of a small cantaloupe. As the bladder expands it extends upward into the abdominal cavity.

URINATION, the process of expelling urine from the bladder (also called micturition), is an involuntary function that becomes an action of learned control. NEURON sensors in the muscle fibers of the bladder wall send NERVE signals to the sacral portion of the SPINAL CORD. This activates the micturition REFLEX, which sends nerve signals via the spinal cord to micturition centers in the BRAIN. These centers activate nerve impulses that cause the urethral sphincter to relax and the detrusor muscle to begin a series of wavelike contractions. These involuntary actions create the urge to urinate, experienced as a sensation of pressure.

Learning to control the pubococcygeal muscle, which forms the floor of the pelvis, serves to override the micturition reflex for a period of time. Relaxing the pubococcygeal muscle and contracting the abdominal muscles synchronize with the involuntary responses of the micturition reflex, and urination occurs. Most children acquire the developmental ability, a blend of conscious effort and neuromuscular maturity, to learn to control urination (commonly called bladder control) between the ages of three and five. With advanced age this control may diminish, a consequence of a weakened urethral sphincter, neurologic conditions, and other factors.

For further discussion of the bladder within the context of the urinary system's structure and

function please see the overview section “The Urinary System.”

HEALTH CONDITIONS THAT CAN AFFECT THE BLADDER

BLADDER CANCER	BLADDER EXSTROPHY
CYSTINURIA	CYSTITIS
CYSTOCELE	NEUROGENIC BLADDER
pyelonephritis	SPINA BIFIDA
URINARY INCONTINENCE	URINARY RETENTION
URINARY TRACT INFECTION (UTI)	URINARY URGENCY
UROLITHIASIS	VESICoureTERAL REFLUX

See also AGING, URINARY SYSTEM CHANGES THAT OCCUR WITH; [BLADDER CATHETERIZATION](#); [CYSTOSCOPY](#); [FECAL INCONTINENCE](#); [KEGEL EXERCISES](#).

bladder cancer The growth of a malignant (cancerous) tumor in the BLADDER. Bladder CANCER may be primary or metastatic (travel to the bladder from a point of origin elsewhere in the body). Doctors diagnose bladder cancer in about 55,000 Americans each year. Bladder cancer is about three times more common in men, and in the United States is the fourth most common cancer among men. Bladder cancer claims about 12,000 lives in the United States each year. The likelihood of developing bladder cancer increases with age.

Cigarette smoking causes about 50 percent of bladder cancers, and exposure to industrial chemicals accounts for another 25 to 30 percent. Among the chemicals known to cause bladder cancer are the aromatic amines: aniline, benzidine, chlornaphazine, methylene dianiline, naphthylamine, and xenylamine. Numerous industries use these chemicals. Tobacco smoke, too, contains aromatic amines.

There are several types of bladder cancers though in the United States one type, transitional-cell CARCINOMA (TCC), accounts for more than 90 percent of bladder cancers. TCC arises from the epithelial (also called urothelial) cells that form the innermost layer of the bladder’s structure and typically undergo a series of predictable cell structure changes before becoming malignant. Other types of bladder cancer are relatively rare and include squamous cell carcinoma, small-cell carcinoma, LYMPHOMA, ADENOCARCINOMA, leiomyosarcoma, and metastatic malignant melanoma. Treatment options and outlook differ among the types of cancer.

Symptoms and Diagnostic Path

Painless HEMATURIA (bloody URINE) is often the earliest indication of bladder cancer. The hematuria may be gross, meaning there is enough BLOOD present to discolor the URINE, or microscopic, detected through urinalysis. Symptoms and signs of bladder cancer may include

- pink, red, or dark brown urine (hematuria)
- DYSURIA (discomfort when urinating)
- URINARY FREQUENCY
- URINARY URGENCY
- sensation of incomplete emptying of the bladder with URINATION

The diagnostic path begins with a standard urinalysis as well as specific urine tests to measure antigens and proteins present in the urine with TCC. These tests include

- NMP22 BladderChek, which detects the presence of nuclear matrix protein (NMP) 22
- BTA-Stat, which detects the presence of bladder tumor antigen (BTA)
- fibrin degradation products (FDPs), which detects the breakdown of blood clots

Further diagnostic procedures include CYSTOSCOPY, INTRAVENOUS PYELOGRAM (IVP), OR COMPUTED TOMOGRAPHY (CT) SCAN to visualize the bladder and urethra to detect tumors, and biopsy (which the urologist typically does during cystoscopy) of identified tumors or suspicious tissue. Biopsy provides the conclusive diagnosis, allowing the pathologist to identify the type of cancer and degree to which it has spread (staging and grading).

Treatment Options and Outlook

The cancer’s type and stage determine treatment options and outlook. Doctors diagnose about 70 percent of TCC in its early stages, when the tumor is small and remains confined to a localized region of the epithelium. These tumors, designated as superficial or stage 0, are highly treatable with minimally invasive therapies that generally preserve the bladder and normal urinary functions. These therapies may include

STAGING OF BLADDER CANCER (TCC)

Stage	Extent of Cancer	Treatment Protocols/Options
0	cancer cells are in a single localized area in the superficial cells of the urothelium (epithelial cells that form the lining of the BLADDER) also called carcinoma in situ (CIS)	one or a combination of <ul style="list-style-type: none">• transurethral resection (TUR) with fulguration (cystoscopic removal of the tumor and electrocautery to the adjacent tissue)• intravesical BCG (bacillus Calmette-Guérin instilled into the bladder via urethral catheter)• intravesical chemotherapy (chemotherapy instilled into the bladder via urethral catheter)• photodynamic therapy
1	tumor remains confined to the urothelium	TUR with fulguration <i>or</i> segmental cystectomy (partial removal of the bladder) in combination with one or more adjunctive therapies: <ul style="list-style-type: none">• intravesical BCG• intravesical CHEMOTHERAPY• radioactive seeding (implantation of radioactive pellets)• systemic chemotherapy
2	tumor extends into but not beyond the detrusor MUSCLE	radical cystectomy (removal of bladder and surrounding organs and tissues in combination with one or more adjunctive therapies: <ul style="list-style-type: none">• RADIATION THERAPY• radioactive seeding• chemotherapy urinary diversion (urostomy, reservoir)
3	tumor extends beyond the bladder wall to surrounding tissue tumor may invade the PROSTATE GLAND (men) or CERVIX, UTERUS, VAGINA, or OVARIES (women)	preoperative chemotherapy radical cystectomy (including removal of lymph nodes and any other organs to which the cancer has spread) urinary diversion postoperative radiation therapy, chemotherapy, or both
4	tumor extends into the structures of the pelvis and abdomen tumor may extend into adjacent lymph nodes metastatic cancer may appear in sites distant from the bladder	preoperative chemotherapy radical cystectomy (including removal of lymph nodes and any other organs or structures to which the cancer has spread) urinary diversion postoperative chemotherapy, radiation therapy, or both alternatively, palliative radiation therapy to shrink the tumors and relieve symptoms
Recurrent	tumor comes back after treatment tumor may recur in the bladder or appear elsewhere in the urinary tract or distant from the bladder	surgery, chemotherapy, radiation therapy or a combination, depending on the cancer's location and previous treatments

- transurethral resection (TUR) with fulguration, a bladder-sparing treatment in which the urologist removes the tumor via cystoscopy and uses electrocautery to burn an area of surrounding tissue to kill any stray cancer cells
- intravesical BCC, in which the urologist instills a solution of bacillus Calmette-Guérin (BCC) to stimulate an IMMUNE RESPONSE that targets any residual cancer cells or isolated cancer cells elsewhere in the urothelium
- intravesical CHEMOTHERAPY, in which the urologist instills chemotherapy drugs into the bladder to target residual cancer cells topically
- photodynamic therapy, in which the person takes a chemical the cancer cells absorb that makes them extraordinarily sensitive to certain frequencies of light

Cancer that spreads into the urothelium or beyond requires more aggressive treatment, typically surgery to remove the tumor and surrounding tissue in combination with chemotherapy, RADIATION THERAPY, or both, and sometimes other therapies such as photodynamic therapy and intravesical BCC. In a segmental cystectomy the urologist removes part of the bladder; in a radical cystectomy the urologist removes all the bladder along with adjacent structures and organs, depending on the extent of the cancer. Segmental cystectomy usually preserves enough of the bladder to retain function and urinary continence.

Radical cystectomy requires further surgery to construct URINARY DIVERSION such as a urostomy, which drains urine continuously into a bag worn attached to the outside of the body, or an internal pouch structured from a loop of intestine that collects urine. With the pouch method, the urologist may be able to fashion a reservoir that collects the urine from the kidneys, and attach it to the urethra for normal continence and urination. When this is not possible or practical, the urologist may be able to construct an opening (stoma) into which the person inserts a catheter to regularly drain urine that collects in the reservoir.

Many of the treatment options for bladder cancer entail significant lifestyle changes. Radical cystectomy and radiation therapy often result in ERECTILE DYSFUNCTION in men, inability to have

vaginal intercourse in women, and sterility in men and women. It is important to fully understand the potential side effects, complications, and QUALITY OF LIFE implications of the various treatment options when making treatment decisions and to obtain a second opinion consultation. Research is ongoing for new therapies, and some people may benefit from participating in clinical trials.

Risk Factors and Preventive Measures

Bladder cancer is very rare in people under age 40. Cigarette smoking and occupational exposure to aromatic amines are the leading causes of bladder cancer, and health experts believe both to be preventable. It appears the highest risk of bladder cancer associated with cigarette smoking is for people who have smoked for several decades. The risk for bladder cancer appears to remain elevated even after stopping smoking. Some health experts believe current and former smokers should have annual urinalysis and urine cytology tests such as NMP22 BladderChek beginning at age 60.

Though exposure-related bladder cancer takes years to decades to develop, researchers believe even brief, limited exposure to aromatic amines may be sufficient to cause damage to the cells of the bladder that later results in bladder cancer. Most people who develop exposure-related bladder cancer have had long-term exposure to aromatic amines, however. Exposure-related bladder cancer generally develops over 15 to 20 years from the time of exposure, though can emerge up to 40 or 50 years later. Strict federal regulations limiting occupational exposure to known carcinogens such as aromatic amines have reduced risk somewhat over the past several decades, though the use of these chemicals remains so pervasive across numerous industries that exposure remains second only to cigarette smoking as a risk factor for bladder cancer.

OCCUPATIONS WITH HIGH AROMATIC AMINES EXPOSURE	
chemical manufacturing	hairdresser
leatherworker	machinist
metalworker	painter
printer	rubber manufacturing
textile worker	

Certain treatments for other cancer may raise the risk for bladder cancer. These include radiation therapy to the pelvic region, notably women who received such treatment for ENDOMETRIAL CANCER or CERVICAL CANCER or men for PROSTATE CANCER, and chemotherapy with cyclophosphamide or ifosfamide. People who have had such treatments should receive ROUTINE MEDICAL EXAMINATION with urinalysis and diagnostic procedures as doctor recommended for early detection of bladder cancer.

See also CANCER TREATMENT OPTIONS AND DECISIONS; LYMPH NODE; METASTASIS; SKIN CANCER; STAGING AND GRADING OF CANCER; SURGERY BENEFIT AND RISK ASSESSMENT.

bladder catheterization The insertion of a narrow, flexible tube into the BLADDER through the URETHRA to drain URINE from the body. Bladder catheterization may be necessary to collect an uncontaminated (sterile) urine sample or to drain urine from the bladder. The catheter placement may be short term, such as after surgery or during serious illness, or long term, such as when STROKE, PARALYSIS, or other condition results in loss of bladder control (complete URINARY INCONTINENCE).

Long-term catheterization may be intermittent, in which the caregiver periodically inserts the catheter to drain collected urine and then removes the catheter, or indwelling (often called a Foley catheter), in which the catheter remains tethered in the bladder (a small inflatable balloon at the tip of the catheter keeps the catheter from sliding out of the urethra). An indwelling catheter drains into a collection bag which the person or caregiver empties frequently and regularly. A caregiver must replace an indwelling catheter every four to six weeks for hygienic reasons. Many people who have indwelling catheters or who use long-term intermittent catheterization take ANTIBIOTIC PROPHYLAXIS to prevent URINARY TRACT INFECTION (UTI). Bladder catheterization greatly increases the risk for UTI. Proper hygiene is essential when inserting and removing a bladder catheter and when an indwelling catheter is in place.

See also CYSTITIS; SPINAL CORD INJURY; TRAUMATIC BRAIN INJURY (TBI).

bladder exstrophy An uncommon CONGENITAL ANOMALY in which the structures of the lower pelvis fail to form properly. As a consequence, the BLADDER protrudes outside the body and may be open or inverted. The URETHRA often fails to close as well. Bladder exstrophy is a random birth defect and is not a hereditary birth defect. About 100 infants are born with bladder exstrophy, which varies widely in severity, each year in the United States.

Treatment in most cases is surgery within several days of birth to reconstruct and reposition the bladder, urethra, symphysis pubis, and other pelvic structures. Most children born with bladder exstrophy require follow-up operations through early childhood and perhaps at PUBERTY when secondary sex characteristics alter the appearance and function of the GENITALIA. However, even with surgical repair or reconstruction the urethral sphincter muscle at the neck of the bladder may not function properly, resulting in incomplete control over the flow of URINE. This URINARY INCONTINENCE may remain throughout life, though there are medical therapies and lifestyle methods to manage the condition. VESICoureteral REFLUX, in which urine flows (refluxes) from the bladder back up the ureters, is also common.

Appropriate reconstructive surgery maintains FERTILITY. Men may experience RETROGRADE EJACULATION, in which SPERM travel inward through the urethra and into the bladder during ejaculation rather than outward through the urethra to exit the PENIS. In such a circumstance a fertility expert can retrieve the sperm and place them into the woman to achieve fertilization. Women born with bladder exstrophy generally are able to carry PREGNANCY to term and deliver vaginally as long as the circumstances of the pregnancy permit.

See also BIRTH DEFECTS; EPISPADIAS.

bladder stone See UROLITHIASIS.

cystinuria An inherited genetic disorder in which the KIDNEYS do not properly reabsorb amino acids collectively called cystine. The excessive excretion of cystine to the URINE causes crystalline calcifications, commonly called stones, to form in the kidneys, ureters, and BLADDER. Most people learn they have the GENE MUTATION, which is autosomal recessive, during analysis of the calcifications. Doctors have known of cystine calcifications in the bladder since the early 1800s. Researchers identified cystinuria as hereditary in the early 1900s and discovered the first effective medication to reduce the formation of cystine calcifications, penicillamine, in the early 1960s. In the late 1990s researchers identified the mutated genes as SLC3A1 on CHROMOSOME 2 and SLC7A9 on chromosome 19.

Pain in the side or back, often on only one side, is the typical symptom of an occlusive (blocking) calcification. The urine may also smell of sulfur (rotten eggs). The diagnostic path may include ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, or MAGNETIC RESONANCE IMAGING (MRI) of the abdomen to visualize the calcifications. Laboratory analysis of fragments filtered from the urine identifies their composition as cystine, confirming the diagnosis. Most of the time the stones pass on their own, though the process often is painful. Doctors usually prescribe ANALGESIC MEDICATIONS for PAIN relief during the time a stone is passing. Occasionally treatments such as EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY (ESWL), which uses high-frequency sound waves to break the calcification into fragments, or surgery (percutaneous nephrolithotomy) are necessary to remove an obstructive and impacted stone.

Because there are as yet no treatments to correct the gene mutation, the cystine calcifications

recur throughout life. Penicillamine, which binds with cystine in the urine to form a compound that easily dissolves in water, remains the medication urologists most often prescribe to reduce the formation of stones. The urologist may also prescribe medications to increase the alkalinity of the urine, such as potassium citrate, which helps dissolve cystine. It is important for people who have cystinuria to drink enough water to maintain good urine output, which dilutes the concentration of cystine and pass it from the body before it forms calcifications. Other lifestyle modifications include decreasing dietary sodium and protein consumption (protein is the source of the cystine).

See also [ENDOSCOPY](#); [FANCONI'S SYNDROME](#); GENE THERAPY; [HYPEROXALURIA](#); INHERITANCE PATTERNS; [NEPHROLITHIASIS](#); SURGERY BENEFIT AND RISK ASSESSMENT; [UROLITHIASIS](#).

cystitis INFLAMMATION of the BLADDER. The most common cause of cystitis is bacterial INFECTION, called URINARY TRACT INFECTION (UTI). Other pathogens, such as fungi (yeasts) and viruses, also can cause infectious cystitis. Nonpathogenic causes of cystitis include irritation of the lining of the bladder, which may occur with excessive consumption of irritating substances such as CAFFEINE, high-acid foods, or certain medications. Cigarette smoking is a significant bladder irritant. RADIATION THERAPY, CHEMOTHERAPY, and AUTOIMMUNE DISORDERS also may cause cystitis. Interstitial cystitis is a chronic condition the hallmark of which is inflammation of the bladder along with a constellation of symptoms for which there are no clearly identifiable causes.

Symptoms and Diagnostic Path

The symptoms of cystitis may include

- DYSURIA (burning or PAIN with URINATION)

- HEMATURIA (bloody URINE)
- URINARY URGENCY
- URINARY FREQUENCY, including NOCTURIA (the need to urinate at night)
- cloudy, foul-smelling, or discolored urine
- pain in the lower abdomen
- pain with SEXUAL INTERCOURSE

The diagnostic path begins with urinalysis, which often shows whether BACTERIA or other pathogens are present in the urine. *Escherichia coli* is the most commonly the culprit for infectious cystitis (UTI). *Chlamydia* and herpes simplex viruses (HSV-1 and HSV-2) are also common causes of UTIs. The urologist may choose further diagnostic procedures such as CYSTOSCOPY or abdominal ULTRASOUND to rule out causes such as tumors or stones (UROLITHIASIS). Cystoscopy allows the urologist to assess bladder capacity, an important factor in determining a diagnosis of interstitial cystitis as reduced bladder capacity is a characteristic of this condition. The current standard of diagnosis for interstitial cystitis further requires the presence of key symptoms over a period of time as well as the exclusion of other causes for the symptoms.

Treatment Options and Outlook

UTIs require therapy with the appropriate medications, such as ANTIBIOTIC MEDICATIONS for bacterial infections or ANTIFUNGAL MEDICATIONS for yeast-based infections. The symptoms of infectious cystitis generally subside within a few days of beginning treatment, and the infection clears with the full course of medication. The oral medication phenazopyridine (Pyridium) acts as a topical anesthetic to block pain signals from the lining of the bladder, easing dysuria until the medication affects the infection. It is essential to take prescribed medications as the doctor directs and to take medications to treat infections until the medication is gone (the full course of treatment) even after symptoms improve. Undertreated or untreated UTIs can migrate from the bladder to the KIDNEYS, where they can cause serious illness and sometimes permanent damage to the kidneys.

Treatment for autoimmune cystitis targets the IMMUNE SYSTEM with ANTIHISTAMINE MEDICATIONS, IMMUNOSUPPRESSIVE MEDICATIONS, and other

approaches that aim to block the inflammatory response. Irritation cystitis often resolves with a combination of increased fluid consumption and ending the cause of the irritation, when possible. Common culprits include coffee, tea, carbonated beverages, citrus fruits and juices, tomatoes and tomato products, chocolate, ALCOHOL, and pickled or smoked foods.

Interstitial cystitis is difficult to treat. People respond differently to treatment regimens, and sometimes a successful treatment becomes ineffective. Urologists may prescribe various kinds of medications to relieve symptoms such as tricyclic ANTIDEPRESSANT MEDICATIONS (which appear to suppress certain pain response mechanisms), NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), and antihistamines. The medication pentosan (Elmiron) is the only oral medication specifically for interstitial cystitis, though women who are pregnant cannot take it. Pentosan also takes up to six months to provide relief and may cause temporary HAIR loss. Other treatments include intravesical therapies in which the urologist instills medications directly into the bladder via urethral catheterization. Bladder distention under ANESTHESIA (via cystoscopy) provides long-term though temporary relief for some people.

FOODS AND DRINKS THAT CAN IRRITATE THE BLADDER

beer	cantaloupe
chocolate	chocolate-covered espresso
coffee	beans
cola beverages	cranberries and cranberry
lemons and lemonade	juice
mixed ALCOHOLIC drinks	onions
oranges and orange juice	peanuts and peanut butter
peppers (sweet or hot)	pineapple
tea (hot or iced)	tomatoes and tomato juice
vinegar and dressings with	wine (white or red)
vinegar	

Risk Factors and Preventive Measures

Women are more likely to develop infectious cystitis and interstitial cystitis, primarily because a woman's shorter URETHRA allows easier access for pathogens. Diligent personal hygiene, including urination soon after sexual intercourse and wiping toilet tissue from front to back, helps reduce exposure to bacteria. Doctors are unsure why intersti-

tial cystitis occurs more often in women. However, doctors do not know what causes interstitial cystitis, either. Finding the cause will likely shed light on all dimensions of this chronic and disruptive condition.

See also [BLADDER CATHETERIZATION](#); [NEPHRITIS](#).

cystocele A hernialike condition in which a woman's [BLADDER](#) bulges into her [VAGINA](#). Cystocele is more common after [MENOPAUSE](#) and in women who have given birth vaginally. It occurs as a consequence of weakened vaginal and pelvic muscles and ligaments that allow the supportive structures for the bladder to relax and the bladder itself to drop. Doctors believe the prime culprit is the intense straining that occurs during vaginal birth, which weakens muscles, coupled with changes in the elasticity of [MUSCLE](#) tissue that take place when levels of [ESTROGENS](#) drop in a woman's body with menopause.

The symptoms of cystocele may include the sensation of vaginal pressure, difficulty urinating, or [URINARY RETENTION](#). Chronic [URINARY TRACT INFECTION](#) (UTI) may also occur, especially when the extent of the cystocele is such that residual [URINE](#) remains in the bladder after [URINATION](#). The doctor can usually diagnose cystocele via vaginal palpation during a [PELVIC EXAMINATION](#), as the sagging bladder causes the vaginal wall to bulge inward. When the diagnosis or the extent of the cystocele is uncertain the doctor may conduct a voiding [CYS-TOURETHROGRAM](#) to determine whether the bladder fully empties with urination.

Mild cystocele that causes no symptoms may require only watchful waiting. The urologist or gynecologist may also recommend a pessary, a device placed within the vagina that gives added support to the vaginal wall. Surgical repair is the treatment of choice for cystocele that interferes with urination, particularly when such interference causes chronic UTI. The surgery tightens the ligaments and muscles of the pelvic floor, restoring support for the bladder. Open surgery requires six to eight weeks for full recovery. Often the surgeon can do the repair laparoscopically, reducing recovery time to two to three weeks.

See also [HYDROCELE](#); [KEGEL EXERCISES](#); [MINIMALLY INVASIVE SURGERY](#); [RECTOCELE](#); [SPERMATOCELE](#); [SURGERY BENEFIT AND RISK ASSESSMENT](#); [VARICOCELE](#).

cystoscopy An endoscopic procedure for visualizing the interior of the [BLADDER](#). The cystoscope is a narrow tube with a tiny light and camera on the tip. Cystoscopy requires no preparation or recovery time and takes place in an outpatient surgery setting under sterile procedures. The urologist anesthetizes the [URETHRA](#), then inserts the cystoscope through the urethra and into the bladder, visualizing the progress on a closed-circuit television monitor. Some people find the insertion mildly uncomfortable. The urologist then injects saline through the cystoscope to fill the bladder, which may create the urge to urinate. However, the bladder must be full to distend its walls for complete examination. Cystoscopy takes 10 to 20 minutes.

Cystoscopy allows the urologist to visualize the interior of the bladder to examine it for signs of [INFLAMMATION](#) or tumors ([BLADDER CANCER](#)). The urologist can use cystoscopy to biopsy suspicious findings, remove bladder stones, and administer medications such as antibiotics or anti-inflammatory drugs. Cystoscopy also allows the urologist to evaluate [BENIGN PROSTATIC HYPERPLASIA](#) (BPH) in men. Some people experience [HEMATURIA](#) ([BLOOD](#) in the urine) and discomfort or burning ([DYSURIA](#)) with [URINATION](#) for a day or two after cystoscopy, a consequence of the cystoscope irritating the urethral tissues. The urologist should evaluate dysuria or hematuria that continues beyond two days as this may indicate a [URINARY TRACT INFECTION](#) (UTI) requiring [ANTIBIOTIC MEDICATIONS](#); the cystoscope may carry [BACTERIA](#) from the [SKIN'S](#) surface into the urethra and bladder.

See also [ENDOSCOPY](#); [UROLITHIASIS](#).

cystourethrogram A diagnostic imaging procedure that shows the flow of [URINE](#) from the [BLADDER](#) through the [URETHRA](#). The radiologist instills a radio-opaque solution (contrast medium) into the bladder through a catheter, then takes a series of X-rays as the solution fills the bladder and urethra. The radio-opaque solution makes these soft tissue structures visible on [X-RAY](#). In a voiding cystourethrogram, the radiologist takes additional X-rays with the person urinating, to visualize the entire flow of urine.

Cystourethrogram shows structural abnormalities, such as narrowing or stricture, of the urethra

and functional problems, such as VESICoureTERAL REFLUX (a condition in which urine flows back into the ureters from the bladder). The procedure requires no preparation or recovery and takes about 20 minutes to complete. Some people experience discomfort during the instillation of the contrast medium because it creates the pressure of a full bladder. Minor discomfort or burning may occur with URINATION for a day or two after the procedure.

See also BENIGN PROSTATIC HYPERPLASIA (BPH); BLADDER CATHETERIZATION; CYSTOSCOPY; URETER; URETHRAL STRICTURE.

dialysis See RENAL DIALYSIS.

dysuria PAIN, discomfort, or burning with URINATION. Dysuria may be primarily external (occur with the passing of URINE through the URETHRA) or internal (felt as discomfort, pressure, or pain within the lower pelvis). Dysuria is most commonly a symptom of CYSTITIS (INFLAMMATION OR

INFECTION of the BLADDER and urethra), though it occurs as a symptom of numerous conditions involving the genitourinary tract. The diagnostic path begins with urinalysis and may include other diagnostic procedures, depending on the full spectrum of symptoms and the findings of the urinalysis. Treatment targets the identified causative condition.

CONDITIONS FOR WHICH
DYSURIA IS A COMMON SYMPTOM

BENIGN PROSTATIC HYPERPLASIA (BPH)	CHLAMYDIA
CYSTITIS	EPIDIDYMITIS
GONORRHEA	NEUROGENIC BLADDER
PELVIC INFLAMMATORY DISEASE (PID)	PROSTATITIS
pyelonephritis	sexual trauma
TRICHOMONIASIS	URETHRITIS
URINARY TRACT INFECTION (UTI)	UROLITHIASIS
VAGINITIS	

See also ANURIA; ENURESIS; HEMATURIA; NOCTURIA; OLIGURIA; URINARY INCONTINENCE; UROLITHIASIS.



end-stage renal disease (ESRD) A condition of permanent RENAL FAILURE in which the KIDNEYS can no longer function to filter wastes from the BLOOD. People who have ESRD require ongoing RENAL DIALYSIS and may be appropriate candidates for KIDNEY TRANSPLANTATION. DIABETES, HYPERTENSION (high BLOOD PRESSURE), and GLOMERULONEPHRITIS are the most common causes of ESRD in the United States. About 300,000 Americans live with ESRD, about 15,000 of whom undergo kidney transplantation each year. ESRD typically follows a period of chronic renal failure that extends for years to several decades. More than 40 percent of Americans who have ESRD are between the ages of 45 to 64.

About a third of people who have ESRD survive five years on renal dialysis, whereas 80 to 90 percent who receive transplanted kidneys live five years after the transplant operation, the five-year marker being a key assessment point for the success of treatment. The waiting list for a cadaver donor kidney (a kidney donated after a person's death) varies widely because donors and recipients must match, and it can be two or three years before one receives a kidney because the supply of donor organs is so limited. An increasingly popular option is living donor transplantation, in which a person (often a family member) who provides a close match for BLOOD TYPE and blood antigens and has two healthy kidneys donates one kidney for transplantation into the person who has ESRD. Each year in the United States nearly 80,000 people die from ESRD.

The U.S. federal government's health-care program for older Americans, Medicare, extends coverage to those of any age who have ESRD. Medicare covers many though not all the costs of renal dialysis and kidney transplantation. Private

health insurance and state-funded programs may provide further benefits for those who qualify.

See also [MEDICARE COVERAGE FOR PERMANENT RENAL FAILURE](#); ORGAN TRANSPLANTATION; SURGERY BENEFIT AND RISK ASSESSMENT.

enuresis An inability to hold the URINE, particularly at night (nocturnal enuresis). A common term for enuresis is bedwetting. Enuresis is primarily a condition of childhood though may persist into adulthood, depending on the cause and treatment efforts. About 85 percent of children are developmentally mature enough to master voluntary control of the bladder sphincter between the ages of 3 and 6. Generally enuresis that persists beyond the age of 12 is either secondary to other physical conditions or psychological in origin. Enuresis is more common among boys.

Conditions commonly associated with enuresis include CYSTITIS, NEUROGENIC BLADDER, and urethral obstruction such as CONGENITAL ANOMALY or obstructive calcifications. Occasionally the cause is damage to the lower SPINAL CORD or to the SPINAL NERVES that control BLADDER function. In teens or adults who develop enuresis, the enuresis may be an early sign of DIABETES or indicate other health conditions such as OBSTRUCTIVE SLEEP APNEA (which disrupts the body's normal sleep rhythms), SEIZURE DISORDERS, or HYPERTHYROIDISM (overactive THYROID GLAND). Obstructive sleep apnea may also be a factor in children between the ages of two and five who have enlarged adenoids, which is a common circumstance among this age group, that block the back of the throat when lying down. Research in the late 1990s suggests some people who have enuresis experience dysfunction of the neurologic interactions that regulate the depth of sleep and initiate sleep arousal.

In some children the causes of enuresis are primarily behavioral, such as ignoring the urge to urinate until it becomes overwhelming, not emptying the bladder immediately before going to bed, or drinking large quantities of fluids throughout the day and especially in the three to four hours preceding bedtime. Generally these behaviors are easy for parents to modify through positive reinforcement and diligent monitoring of the child's drinking and URINATION patterns. Psychological enuresis typically occurs due to profound emotional distress and is not the result of conscious behavior.

Enuresis becomes a significant embarrassment to most who have it after they reach about the age of 8 to 10 and especially for teens and adults. Children may refuse to spend the night with friends or have friends spend the night with them and may avoid overnight activities such as camping or vacationing in motels. Their refusal may be overt or they may express unreasonable fears.

Symptoms and Diagnostic Path

The symptom of enuresis is inappropriate urination, often during naps or when sleeping at night, but it may occur any time. The diagnostic path consists of a careful history of eating, drinking, urination, and bowel habits as well as patterns of enuresis (such as all the time or only during sleep). The urologist may conduct diagnostic procedures such as urinalysis, ULTRASOUND of the bladder, voiding CYSTOURETHROGRAM, or CYSTOSCOPY, depending on the suspected underlying cause. In most situations in which the urinalysis is normal, however, the urologist delays extensive diagnostic procedures until after a trial of basic treatment and behavioral interventions.

Treatment Options and Outlook

Treatment may combine medical interventions with behavioral approaches such as limiting fluids in the evening and fully emptying the bladder right before going to bed. Enuresis alarms (moisture-sensitive devices) are especially effective for children. Medication therapy may include desmopressin (DDAVP), which decreases urine production, or oxybutynin (Ditropan) or tolterodine (Detrol), medications that slow smooth muscle stimulation.

Risk Factors and Preventive Measures

Nocturnal enuresis appears to run in some families, though researchers are not sure what accounts for this. The key risk factors for enuresis are organic causes such as congenital anomalies or physiologic dysfunctions and severe emotional stress. Health experts stress that neither punishment nor the so-called bladder training method (holding a full bladder for a determined amount of time, ostensibly to strengthen sphincter control) is effective in ending enuresis. These approaches fail to address the causes of enuresis, result in further embarrassment and discomfort, and may exacerbate the underlying cause of the enuresis. Time, patience, and positive reinforcement (such as praise and small rewards) as well as appropriately addressing any physiologic dysfunctions, result in ending enuresis about 98 percent of people.

See also [ANURIA](#); [CONGENITAL ANOMALY](#); [DYSURIA](#); [HEMATURIA](#); [NEURAL TUBE DEFECTS](#); [NOCTURIA](#); [OLIGURIA](#); [SLEEP DISORDERS](#); [URINARY INCONTINENCE](#); [URINARY URGENCY](#).

epispadias A random CONGENITAL ANOMALY in which the URETHRA forms incorrectly. Epispadias often occurs as an element within a constellation of congenital malformations involving the pelvic structures (including the pelvic bones) and the GENITALIA.

In boys the urethra may exit the PENIS other than at the tip or appear as an open channel that runs the length of the PENIS, and often occurs in conjunction with CHORDEE (a deformity in which the penis curves sharply). In girls the urethra may exit anywhere between the neck of the BLADDER and the upper labial fold, and typically occurs in conjunction with genital deformities such as bifid (two-fold or split) CLITORIS and abnormalities of the VULVA.

Epispadias is rare in either sex though much more so in girls, and typically apparent at birth. Early surgery is the preferred means to correct the defects, which preserves FERTILITY and sexual function, restores the genitalia to normal appearance, and helps establish urinary continence (the ability to control the flow of URINE). Prenatal ULTRASOUND sometimes can detect epispadias before birth. There are no measures to prevent epispadias.

See also [BIRTH DEFECTS](#); [BLADDER EXSTROPHY](#); [HYPOSPADIAS](#); [PRENATAL CARE](#).

extracorporeal shock wave lithotripsy (ESWL)

A therapeutic procedure in which a machine called a lithotripter generates shock waves that cause calcifications within the urinary tract, commonly called kidney stones (NEPHROLITHIASIS) or bladder stones (UROLITHIASIS), to break apart into smaller fragments the URINE can carry out of the body. Lithotripsy became available in 1980 and has evolved into the current treatment of choice for stones smaller than 2 centimeters (about 0.75 inch) in diameter that form in the KIDNEYS, URETER, and BLADDER. ESWL is sometimes effective for gallstones (cholelithiasis) as well. Today there are several types of lithotriptors, each of which uses a different energy source though all apply the same basic approach which is to focus a pulse of intense energy (the shock wave) at the stone.

Women who are or could be pregnant should not undergo ESWL.

Typically preparation requires having nothing to eat or drink for six hours before the scheduled time of the procedure. The urologist or nephrologist may recommend stopping routine use of NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), aspirin, and anticoagulation medications for 7 to 10 days before the scheduled ESWL to reduce the risk of bleeding during or after the procedure, as these medications interfere with PLATELET AGGREGATION and prolong the length of time a BLOOD clot takes to form. ESWL takes about an hour to perform, with about two hours in the recovery room afterward. The person undergoing ESWL treatment will need someone to take him or her to and from the treatment center.

Procedure

The urologist or radiologist generally gives the person an anesthetic or sedative for comfort before the ESWL begins. The pressure of the shock waves coming in contact with the stones can be uncomfortable. The lithotripter integrates FLUOROSCOPY or ULTRASOUND to pinpoint the location of the targeted stone and can target several stones in one ESWL session. The person wears a hospital gown and lies on a cushioned table. The ESWL technician positions the lithotripter over the person to deliver the shock waves, with continual

monitoring and adjustment to maintain accurate focus. The radiologist or urologist makes sure the person has adequate ANESTHESIA OR SEDATION to remain comfortable for the duration of the procedure.

Risks and Complications

The most common risk associated with ESWL is bleeding from the tissues around the site of the stone, resulting in HEMATURIA (bloody urine) and some discomfort. Many people experience discomfort for up to several days after the ESWL, for which the urologist prescribes ANALGESIC MEDICATIONS (pain relief). Most people should plan on taking it easy for a few days after ESWL. It may take days to weeks for all of the fragments to pass, and larger fragments may cause pain when they pass. Sometimes fragments of the stone cluster in the ureter or URETHRA, temporarily blocking the flow of urine and causing considerable PAIN. Generally movement (such as walking) and drinking lots of fluids help flush these clusters from the body, with appropriate analgesic medication to mitigate the pain. Some people require several ESWL sessions to completely disperse all of the stones and fragments.

Outlook and Lifestyle Modifications

Once the stone breaks apart and the fragments pass from the body in the urine, no further treatment for the stone is necessary. The urologist or nephrologist may recommend dietary changes, increased physical activity, increased water consumption, and sometimes medications to help prevent new stones from forming. Such factors depend on the stone's content and the person's medical history, including other health conditions. Both kidney stones and bladder stones tend to recur.

See also [CYSTINURIA](#); [GALLBLADDER DISEASE](#); [SURGERY BENEFIT AND RISK ASSESSMENT](#).

Fanconi's syndrome A dysfunction of the KIDNEYS in which the renal tubules do not function properly, resulting in a constellation of diverse symptoms. The renal tubule, a structure of the kidney's filtering mechanism within the NEPHRON, filters many substances from the BLOOD to retain those the body needs and excrete those the body

does not need. In Fanconi's syndrome, the renal tubule excretes into the URINE numerous vital substances it should retain in the blood. Among these substances are GLUCOSE, uric acid, calcium, magnesium, potassium, phosphate, and amino acids. The renal tubule also excretes excessive water into the urine.

Numerous GENETIC DISORDERS cause Fanconi's syndrome. Among the most common are metabolic conditions that affect the body's ability to use or store substances such as cystine, glycogen, fructose, and tyrosine. HEAVY-METAL POISONING, such as from lead or mercury, and DRUG toxicity account for most acquired Fanconi's syndrome. Conditions such as AMYLOIDOSIS, in which protein deposits accumulate in organs such as the kidneys, also can damage the renal tubules to cause Fanconi's syndrome. The syndrome occasionally develops in people who undergo KIDNEY TRANSPLANTATION.

Equally numerous symptoms can suggest Fanconi's syndrome and may appear initially to be unrelated. In children the most common symptoms are stunted growth, BONE deformities similar to those which occur in RICKETS, and MUSCLE weak-

ness. In adults, the most common symptoms are spontaneous FRACTURE, electrolyte imbalance, and serum acidosis (increased acidity of the blood). General symptoms sometimes present in children or adults include excessive thirst and URINATION, CONSTIPATION, and DEHYDRATION. Blood and urine tests identify the depletions and excesses of the substances the renal tubules are failing to reabsorb.

Treatment targets the underlying cause when doctors can identify it and the resulting conditions when the underlying cause remains unknown (idiopathic Fanconi's syndrome). Doctors can treat many genetic disorders of METABOLISM from early childhood, forestalling or preventing complications such as Fanconi's syndrome. With appropriate treatment kidney function can return to normal. Untreated Fanconi's syndrome can progress to END-STAGE RENAL DISEASE (ESRD), requiring long-term RENAL DIALYSIS or kidney transplantation.

See also [CYSTINURIA](#); ENVIRONMENTAL HAZARD EXPOSURE; MINERALS AND HEALTH; OSTEOPOROSIS; [WILSON'S DISEASE](#).



glomerulonephritis INFLAMMATION of the glomeruli within the nephrons of the KIDNEYS. The glomerulus is the coiled capillary network through which BLOOD circulates for filtration. Glomerulonephritis, also called glomerular disease, may be acute (come on suddenly) or chronic (develop slowly over time). Acute glomerulonephritis is often a temporary condition that improves with treatment and causes minimal or no residual damage to the glomeruli. Chronic glomerulonephritis tends to be progressive, eventually deteriorating to RENAL FAILURE and END-STAGE RENAL DISEASE (ESRD). INFECTION, AUTOIMMUNE DISORDERS, NEPHROPATHY of DIABETES, and nephropathy of HYPERTENSION (high BLOOD PRESSURE) are the most common identified causes of glomerulonephritis. As often as not, however, the nephrologist cannot determine the cause and focuses instead on treatment.

Symptoms and Diagnostic Path

The symptoms of glomerulonephritis may be minimal and difficult to detect or obvious and debilitating, depending on whether the condition is chronic or acute. Common symptoms of glomerulonephritis include

- fatigue
- edema (swelling or puffiness) of the face, hands and wrists, and feet and ankles
- discolored URINE (commonly described as tea-colored or cola-colored)
- hypertension
- foamy urine (ALBUMINURIA)

The diagnostic path begins with urinalysis, which typically reveals HEMATURIA (blood in the urine) and albuminuria (excessive ALBUMIN, or

protein, in the urine). In many people, urinalysis done as part of a ROUTINE MEDICAL EXAMINATION provides the first indication of glomerulonephritis. Blood tests help the nephrologist assess the ability of the kidneys to remove toxins and wastes from the blood. Imaging procedures such as abdominal ULTRASOUND or COMPUTED TOMOGRAPHY (CT) SCAN can show the damage to the glomeruli. Needle biopsy of the kidney tissue allows microscopic examination of the glomeruli, providing the definitive diagnosis.

Treatment Options and Outlook

Treatment targets either the underlying condition or the resulting symptoms. Because hypertension is nearly always either a cause or a consequence of glomerulonephritis, the doctor is likely to prescribe medications that lower blood pressure (antihypertensives) such as beta blockers, angiotensin-converting enzyme (ACE) inhibitors, or calcium channel blockers. The doctor may also prescribe medications to extract more water from the blood (diuretics), which lowers blood pressure as well as eases the workload of the kidneys. Bacterial infections require ANTIBIOTIC MEDICATIONS. Viral infections, which are fairly common, will run their course after which kidney function usually returns to normal.

Acute glomerulonephritis may result in renal failure, requiring short-term RENAL DIALYSIS to remove wastes and toxins from the blood until kidney function returns enough to resume this functions. CORTICOSTEROID MEDICATIONS and other immunosuppressive therapies are necessary when the cause of the glomerulonephritis is an autoimmune disorder. Once the cause of the inflammation resolves, the glomerulonephritis generally resolves as well, and kidney function returns to normal.

Chronic glomerulonephritis may require long-term medication therapy, and presents a significant risk for progression to ESRD despite treatment.

Risk Factors and Preventive Measures

Diabetes and hypertension are the leading risk factors for glomerulonephritis. Keeping these conditions under control with medications and lifestyle methods lowers the likelihood for damage to the kidneys and can slow the progression of chronic glomerulonephritis. Untreated or undertreated (failing to complete the full course of antibiotics) strep infections such as STREP THROAT OR IMPETIGO remain a significant source of bacterial infection that causes glomerulonephritis. Though there are no methods for preventing glomerulonephritis, the doctor may recommend measures to slow its progression such as dietary modifications (less sodium, potassium, and protein; more water consumption).

See also [GOODPASTURE'S SYNDROME](#); [MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE](#); [NEPHRITIS](#); [NEPHRON](#); [NEPHROTIC SYNDROME](#); [POLYARTERITIS](#); [SYSTEMIC LUPUS ERYTHEMATOSUS \(SLE\)](#).

glomerulosclerosis The formation of SCAR tissue (fibrosis) within the glomeruli, the coiled capillary networks within the nephrons of the KIDNEYS. The most common presentation of glomerulosclerosis is focal segmental glomerulosclerosis in which the fibrosis is scattered throughout the glomeruli, affecting only parts of the GLOMERULUS in various nephrons. The damage permanently blocks the affected glomeruli, however. Because the kidneys have millions of nephrons, glomerulosclerosis may be under way for a significant time before it causes enough damage to manifest symptoms. Some forms of glomerulosclerosis are familial (have a hereditary component) and others arise in conjunction with INFECTION such as HIV/AIDS. Most often, however, the glomerulosclerosis is idiopathic—the nephrologist can find no cause for the scarring. Though some researchers believe the cause is autoimmune, glomerulosclerosis does not respond to IMMUNOSUPPRESSIVE THERAPY.

Symptoms and Diagnostic Path

Early symptoms of glomerulosclerosis are vague and may not appear to be symptoms at all. They include

- poor APPETITE in combination with weight gain
- edema (swelling) of the face, hands and wrists, and feet and ankles
- foamy URINE, indicating ALBUMINURIA (excretion of ALBUMIN, a form of protein, in the urine)
- discolored urine, indicating HEMATURIA (BLOOD in the urine)

The diagnostic path begins with urinalysis, which typically reveals the albuminuria as well as hematuria. Needle biopsy of the kidney shows the fibrosis among the glomeruli and may also show the presence of immunoglobulins characteristic of the condition. HYPERTENSION (high BLOOD PRESSURE) is also often present, a consequence of damage that affects the parts of the NEPHRON that produce a key HORMONE essential for blood pressure regulation (RENIN). Because the kidneys also produce ERYTHROPOIETIN (EPO), the hormone that stimulates the BONE MARROW to produce erythrocytes (red blood cells). Erythrocytes carry oxygen in the blood circulation. Progressive glomerulosclerosis often results also in ANEMIA (insufficient oxygen in the blood circulation).

Treatment Options and Outlook

There is no cure for glomerulosclerosis, which in most people progresses over about 10 years to END-STAGE RENAL DISEASE (ESRD). Treatment includes medications to control blood pressure. As CHOLESTEROL BLOOD LEVELS also tend to be high (HYPERLIPIDEMIA), the doctor may prescribe medications and lifestyle changes to help bring them down. These therapies may slow the progression of the fibrosis. The progressive loss of protein further damages the nephrons. At the point of ESRD, long-term RENAL DIALYSIS OR KIDNEY TRANSPLANTATION is necessary to sustain life.

Risk Factors and Preventive Measures

Glomerulosclerosis, particularly focal segmental, tends to develop in people who are in their 20s and 30s and is about three times more common among African American males. There are no measures to prevent glomerulosclerosis. Managing the symptoms as effectively as possible may delay the onset of ESRD. Kidney transplantation becomes the treatment option that offers the greatest opportunity for a return to normal activities.

See also [GLOMERULONEPHRITIS](#); [MEDICARE COVERAGE FOR PERMANENT RENAL FAILURE](#); [NEPHROTIC SYNDROME](#).

glomerulus The coiled capillary network within the [NEPHRON](#) of the kidney through which [BLOOD](#) passes for filtration. Glomeruli are abundant within the [KIDNEYS](#) as each kidney contains more than a million nephrons. The walls of the glomerulus are only a few cells in thickness. The glomerular walls are semipermeable, allowing smaller molecules such as water, metabolic wastes, [GLUCOSE](#), and electrolytes to pass through and collect in the capsule (called Bowman's capsule) that surrounds the glomerulus. Together the glomerulus and Bowman's capsule are the renal corpuscle. The fluid and its contents, called filtrate, passes into the tubules of the nephron, which further filter and concentrate the filtrate. The nephron eventually reabsorbs 99 percent of the filtrate back into the blood; the remaining fluid drains into collecting ducts to move out of the kidneys as [URINE](#). The glomerular filtration rate (GFR) is an important measure of kidney function. The GFR of a healthy adult kidney is 125 milliliters per minute.

For further discussion of the glomerulus within the context of the urinary system's structure and function please see the overview section "The Urinary System."

See also [GLOMERULONEPHRITIS](#); [GLOMERULOSCLEROSIS](#); [RENAL FAILURE](#).

Goodpasture's syndrome An autoimmune disorder in which the [IMMUNE SYSTEM](#) produces antibodies that attack the glomeruli in the [KIDNEYS](#), impairing kidney function, and the alveoli in the [LUNGS](#), causing bleeding into the lung tissue. In most people who develop Goodpasture's syndrome the symptoms follow a viral [INFECTION](#) of the upper respiratory tract or exposure to environmental toxins, notably hydrocarbons. Because Goodpasture's syndrome tends to run in families, researchers believe a [GENE MUTATION](#) is likely responsible.

Siphoning gasoline and sniffing aerosols such as paints and glues are the most common exposures to hydrocarbons that can result in Goodpasture's syndrome.

Though the coughing up of bloody [SPUTUM](#) ([HEMOPTYSIS](#)) is the first and often the more distressing sign of Goodpasture's syndrome, [GLOMERULONEPHRITIS](#) is the more serious consequence, leading rapidly in many people to [RENAL FAILURE](#). [ANEMIA](#) (insufficient erythrocytes in the blood) and [HYPERTENSION](#) (elevated [BLOOD PRESSURE](#)), consequences of the renal failure, may quickly become significant.

SYMPTOMS OF GOODPASTURE'S SYNDROME

Pulmonary (Lungs)	Renal (Kidneys)
HEMOPTYSIS (bloody SPUTUM)	HEMATURIA (bloody URINE)
DYSPNEA (shortness of breath)	foamy urine (indicates ALBUMINURIA)
COUGH	decreased urine volume
CHEST PAIN	edema (fluid retention)

The diagnostic path includes blood and urine tests to assess kidney function, chest [X-RAY](#) to detect accumulated fluid in the lungs, and biopsy of lung and kidney tissue to confirm the presence of antibodies. The course of Goodpasture's syndrome may run two months to several years. Early diagnosis allows aggressive interventions, including plasmapheresis to remove antibodies from the bloodstream and [IMMUNOSUPPRESSIVE THERAPY](#) to prevent the immune system from producing further antibodies. These interventions can mediate the syndrome's progression, minimizing damage to the kidneys. Though about 90 percent of those who develop this once-fatal syndrome now survive, many of them continue to experience progressive renal failure that results in [END-STAGE RENAL DISEASE \(ESRD\)](#).

See also [ALVEOLUS](#); [ANTIBODY](#); [AUTOIMMUNE DISORDERS](#); [HEMAPHERESIS](#); [GLOMERULUS](#); [RENIN](#).



hematuria BLOOD in the URINE. Hematuria may result from numerous circumstances and always requires medical evaluation to determine the underlying cause. Though BLADDER CANCER is uncommon, hematuria often is the earliest sign of its presence. Gross hematuria occurs when the amount of blood in the urine is sufficient to discolor the urine (typically pink, red, or brown). Occult, or microscopic, hematuria occurs when the amount of blood in the urine is very slight, detected during microscopic examination of the urine.

Urinalysis is the first step of the diagnostic path, with additional diagnostic procedures, depending on the findings and the symptoms. Treatment targets the underlying cause. Certain medications or foods may cause the urine to be pink or red, in which case the urinalysis shows there to be few erythrocytes (red blood cells) present in the urine. MENSTRUATION may also give the appearance of blood in the urine.

**CONDITIONS FOR WHICH
HEMATURIA IS A COMMON SYMPTOM**

BENIGN PROSTATIC HYPERPLASIA (BPH)	BLADDER CANCER
BLUNT TRAUMA to the abdomen or back	CHLAMYDIA
CYSTITIS	EPIDIDYMITIS
GENITAL TRAUMA	GONORRHEA
PROSTATITIS	pyelonephritis
TRICHOMONIASIS	URETHRITIS
URINARY TRACT INFECTION (UTI)	UROLITHIASIS

See also ANURIA; DYSURIA; ENURESIS; NOCTURIA; OLIGURIA.

hemolytic uremic syndrome RENAL FAILURE that occurs as a rare complication in children after INFECTION with *Escherichia coli* O157:H7 acquired

from contaminated food. *E. coli* O157:H7 causes hemorrhagic ENTERITIS, itself a life-threatening infection. Hemolytic uremic syndrome occurs when the toxins the *E. coli* O157:H7 release enter the bloodstream. The toxins destroy erythrocytes (red BLOOD cells) and platelets (clotting cells). Remnants of the destroyed blood cells clog the glomeruli within the KIDNEYS, preventing blood from flowing through these filtering structures. As more glomeruli become affected, the kidneys can no longer filter toxins from the blood.

Symptoms and Diagnostic Path

The symptoms of hemolytic uremic syndrome begin to emerge as the child appears to be recovering from the enteritis. The earliest indication of hemolytic uremic syndrome is the appearance of PETECCHIAE, pinpoint hemorrhages under the surface of the SKIN, in a child recovering from *E. coli* O157:H7 hemorrhagic enteritis. Other symptoms include reduced URINE volume, fatigue, irritability, and pale skin. Blood tests typically show the damaged blood cells and indications of diminishing kidney function. However, the child becomes life-threateningly ill very rapidly, requiring immediate hospitalization and intensive medical treatment.

Treatment Options and Outlook

There is no cure for hemolytic uremic syndrome. Treatment consists of intensive supportive care while the condition runs its course, including efforts to maintain the child's fluid and electrolyte balances as well as RENAL DIALYSIS to filter toxins from the blood. The renal failure disrupts all body systems and functions, often causing severe HYPERTENSION (high BLOOD PRESSURE), other cardiovascular problems, LIVER dysfunction, and neurologic dysfunction. With prompt and aggressive medical

care, 80 percent of children survive. About 70 percent of them recover fully with no residual health problems. Among the other 30 percent renal failure progresses to END-STAGE RENAL DISEASE (ESRD), often within months though sometimes over several years, requiring long-term renal dialysis and ultimately KIDNEY TRANSPLANTATION.

Risk Factors and Preventive Measures

Hemolytic uremic syndrome is a rare complication of *E. coli* O157:H7 hemorrhagic enteritis, so any child who acquires this infection incurs the risk for the syndrome. There are no measures to prevent hemolytic uremic syndrome as a complication of *E. coli* O157:H7 infection. Even with prompt and aggressive medical care for the hemorrhagic enteritis, hemolytic uremic syndrome remains a potential complication. The most effective preventive measures are precautions to protect against *E. coli* O157:H7 infection. Such measures include

- wash hands with hot, soapy water before and after handling meats
- do not handle other foods when preparing meats
- use separate, nonporous surfaces and utensils (not wooden) to prepare meats for cooking
- wash food preparation surfaces and utensils with hot soapy water immediately after preparing meats
- thoroughly cook all meats to the recommended temperatures for the kind of meat
- thoroughly rinse all fruits and vegetables in cold running water before eating or preparing them

See also FOOD-BORNE ILLNESSES; [GLOMERULUS](#).

hepatorenal failure The progressive failure of the KIDNEYS in people who have chronic LIVER FAILURE. Doctors do not know what causes hepatorenal failure, also called hepatorenal syndrome, to develop though they do know the BLOOD supply to the kidneys becomes suddenly and severely restricted. Not enough blood flows through the kidneys for the kidneys to filter waste byproducts and toxins from the blood, and these substances

accumulate in the blood. Because the kidneys play key roles in regulating BLOOD PRESSURE, HYPERTENSION (elevated blood pressure) may also develop.

The primary symptom of hepatorenal failure is diminished URINE production in a person who has chronic liver failure. Symptoms of liver failure are also often present and typically include ASCITES (fluid retention in the abdominal cavity), JAUNDICE (yellowish discoloration of the skin), and abnormal bleeding. Blood and urine tests help evaluate liver and kidney function, and diagnostic imaging procedures such as abdominal ULTRASOUND OR COMPUTED TOMOGRAPHY (CT) SCAN demonstrate the extent of physical damage to the liver and the kidneys.

Treatment aims to improve both liver and kidney functions. RENAL DIALYSIS often becomes necessary. In some people the kidneys remain healthy and return to full function when the underlying liver disease improves, such as might occur with LIVER TRANSPLANTATION. When liver disease is severe, however, the progressive failure of the kidneys means the body loses nearly all of its ability to remove toxins and the risk of death is very high.

See also [CIRRHOSIS](#); COAGULATION; ENCEPHALOPATHY; LIVER DISEASE OF ALCOHOLISM.

horseshoe kidney A random CONGENITAL ANOMALY in which a band of tissue fuses the KIDNEYS at the bottom, forming a shape resembling a horseshoe. The tissue band, called an isthmus, may be fibrous or the same tissue as the kidneys. In most people who have this anomaly, both kidneys are fully functional. However, the fusion distorts the normal structure of the kidneys, leading over time to conditions such as HYDRONEPHROSIS (dilation of the renal pelvis), NEPHROLITHIASIS (kidney stones), and VESICoureteral REFLUX (backflow of URINE from the BLADDER into the ureters and kidneys). The BLOOD vessels that supply the horseshoe kidney are often intertwined and anomalous, providing abnormal blood flow to the fused kidney that can affect its functions. The horseshoe kidney also resides lower in the abdominal cavity, placing it outside the protective enclosure of the rib cage. Horseshoe kidney increases the risk for some types of primary RENAL CANCER.

Two thirds of people who have horseshoe kidney learn of the anomaly during diagnostic proce-

dures for other health concerns. Doctors diagnose most others in the course of identifying the causes for conditions that affect the kidneys. When symptoms do occur, they generally represent a consequential condition such as nephrolithiasis. The diagnostic path includes blood and urine tests to assess kidney function. Diagnostic imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN or renal ULTRASOUND can provide visual evidence of the fused kidneys. Diagnostic prenatal ultrasound often detects horseshoe kidney in the unborn child.

For the most part horseshoe kidney of itself presents no unusual health risks. The fused kidneys are prone to the same conditions that affect kidneys in general. Treatment targets any conditions affecting the kidney. The urologist or nephrologist may suggest surgery (nephroplasty) to separate the kidneys and establish normal positioning of the ureters and the blood supply. Watchful waiting, with routine medical care to monitor kidney function and health, is appropriate for many people who have no symptoms of kidney disease. Researchers do not know what causes horseshoe kidney to occur. One child born with horseshoe kidney does not increase the likelihood that other children will also have the anomaly; the condition appears to be entirely random.

See also [EPISPADIAS](#); [HYPOSPADIAS](#); [TURNER'S SYNDROME](#).

hydronephrosis A circumstance in which the renal pelvis, the portion of the kidney that collects URINE for passage from the kidney via the URETER, dilates and enlarges. Hydronephrosis results from conditions of the kidney that slow or block the flow of urine, causing urine to back up into or pool in the renal pelvis. Such conditions may include obstructive NEPHROLITHIASIS (kidney stones that block the ureter), NEUROGENIC BLADDER (in which the BLADDER fails to respond to the normal neurosensory signals that regulate URINATION and becomes overly full), and VESICOURETERAL REFLUX (urine washes back into the ureters from the bladder).

Unilateral hydronephrosis, which affects only one kidney, is the more common presentation. Bilateral hydronephrosis, which affects both KIDNEYS, often indicates CONGENITAL ANOMALY of kidney

or ureteral structure though may develop as a consequence of conditions such as HYPERTENSION (high BLOOD PRESSURE), DIABETES and BENIGN PROSTATIC HYPERPLASIA (BPH) that constricts the urethra and slows the flow of urine during urination.

The symptoms of hydronephrosis may include

- abdominal or back PAIN
- DYSURIA (discomfort or burning with urination)
- URINARY FREQUENCY
- URINARY URGENCY
- signs of INFECTION such as FEVER and cloudy or bloody urine

Some people may have no symptoms, with the hydronephrosis showing up during evaluation of other medical concerns or in PREGNANCY. The diagnostic path begins with urinalysis and blood tests to evaluate kidney function and usually includes an abdominal X-RAY, ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, INTRAVENOUS PYELOGRAM (IVP), or MAGNETIC RESONANCE IMAGING (MRI) examination to visualize the kidneys. Treatment targets the underlying disease process to restore the free flow of urine. Untreated hydronephrosis results in permanent damage to the kidney that may lead to RENAL FAILURE.

See also [HEMATURIA](#); [HORSESHOE KIDNEY](#); [NEPHRITIS](#); [NOCTURIA](#); [URINARY TRACT INFECTION \(UTI\)](#).

hypercalciuria Excessive excretion of calcium in the URINE. About 80 percent of people who have kidney stones (NEPHROLITHIASIS) or BLADDER STONES (UROLITHIASIS) have hypercalciuria. In most people the circumstance appears a combination of factors that typically include high dietary calcium intake, insufficient water consumption (resulting in low urine volume), and physical inactivity. The water and citrate content of the urine normally allows most of the calcium the KIDNEYS extract from the BLOOD to dissolve and pass from the body. When urine volume and citrate concentration are low, calcium in the urine combines with other minerals (usually oxalate or phosphate) to form crystalline structures. Over time these structures harden or calcify (called calculi). Inactivity contributes to calculus formation because it allows mineral sediments to settle, facilitating their crystallization.

Other causes of hypercalciuria include endocrine disorders such as [HYPERPARATHYROIDISM](#) and [ADDISON'S DISEASE](#), kidney dysfunction, and [MALABSORPTION](#) disorders of the gastrointestinal system. Many people who have hypercalciuria do not have nephrolithiasis or urolithiasis, though the presence of excess calcium in the urine raises their risk for developing either condition. Routine urinalysis often detects hypercalciuria. Doctors generally recommend increased water consumption, maintaining dietary calcium intake at recommended levels for [BONE](#) health, and daily physical activity. Many people also benefit from thiazide diuretic medications, which act to slow the extraction of calcium in the kidneys as well as to increase the volume of urine. Many stones that form as a consequence of hypercalciuria will pass through the urinary tract without medical intervention, though they require treatment when they cause significant pain or an obstruction in the kidney, [URETER](#), bladder, or [URETHRA](#).

See also [CYSTINURIA](#); [FANCONI'S SYNDROME](#); [HYPER-OXALURIA](#); [RENAL TUBULAR ACIDOSIS](#).

hyperoxaluria Excessive [OXALATE](#) excretion in the [URINE](#). Oxalate is a natural chemical that enters the body through dietary sources such as vegetables, fruits, and grains. The [LIVER](#) also metabolizes oxalate. Researchers do not know what benefits the body derives from oxalate. However, in the body oxalate attracts calcium, creating the insoluble compound calcium oxalate. About 80 percent of kidney stones are made of calcium oxalate. Deposits of calcium oxalate may also accumulate in tissues such as the [KIDNEYS](#), liver, [HEART](#), and bones, a circumstance known clinically as oxalosis.

Most hyperoxaluria is idiopathic (without a clearly identifiable cause). Doctors believe about 50 percent of people who have mild to moderate hyperoxaluria consume an abundance of foods high in dietary oxalate. In some people the binding between calcium and oxalate intensifies for reasons researchers do not understand though believe results from genetic factors. Less commonly, hyperoxaluria occurs as an autosomal recessive genetic disorder that results in the absence of an enzyme the body requires to break down oxalate into soluble components that are more easily excreted. Genetic hyperoxaluria gen-

erally causes symptoms (typically kidney or bladder stones) in early childhood. Rarely, hyperoxaluria is a secondary complication of [MALABSORPTION](#) disorders, such as [SHORT BOWEL SYNDROME](#) and [INFLAMMATORY BOWEL DISEASE \(IBD\)](#), that alter the gastrointestinal tract's absorption of dietary calcium and oxalate.

The most common symptoms are kidney stones ([NEPHROLITHIASIS](#)) or bladder stones ([UROLITHIASIS](#)). The diagnostic path includes laboratory tests to measure the levels of oxalate in the urine and the [BLOOD](#), analysis of any stones, and family history. Dietary modifications (eating fewer foods with high oxalate content) are often treatment enough for mild idiopathic hyperoxaluria. Other therapeutic approaches include medications to increase the ability of the urine to dissolve calcium and oxalate salts, magnesium and pyridoxine (vitamin B₆) supplementation, and increasing water consumption to dilute the urine. Primary (genetic) hyperoxaluria typically results in [RENAL FAILURE](#) by early adulthood with the only definitive treatment being [KIDNEY TRANSPLANTATION](#).

See also [ADDISON'S DISEASE](#); [HYPERCALCIURIA](#); [HYPERPARATHYROIDISM](#); [ORGAN TRANSPLANTATION](#); [SURGERY BENEFIT AND RISK ASSESSMENT](#).

hypospadias A [CONGENITAL ANOMALY](#) in which the [URETHRA](#) is shorter than normal and exits along the underside of the [PENIS](#) in a boy or into the [VAGINA](#) in a girl. Though uncommon overall, hypospadias is very rare in girls. In boys, [CHORDEE](#) (severely curved penis) often accompanies hypospadias. The preferred treatment is surgery to extend the urethra to its normal length and path. In boys, such surgery also includes correction of the [chordee](#). The surgery establishes normal [URINATION](#) and, in boys, restores structural integrity to the penis that will permit sexual function and [FERTILITY](#) later in life. The urologist typically performs the [OPERATION](#) when the child is between 6 and 12 months of age. More than 90 percent of such corrective surgery produces a functionally and cosmetically acceptable repair. Some children may need more than one operation, notably boys in whom the urethral opening is near the base of the penis.

See also [BIRTH DEFECTS](#); [BLADDER EXSTROPHY](#); [EPISPADIAS](#).

interstitial cystitis See [CYSTITIS](#).

intravenous pyelogram (IVP) A diagnostic imaging procedure to evaluate the flow of BLOOD and URINE through the KIDNEYS, ureters, BLADDER, and URETHRA. IVP requires moderate preparation that typically includes taking a laxative the night before the scheduled procedure to empty the intestines so the IVP provides clear visualization of the renal structures and then consuming nothing by mouth until after the IVP. An IVP takes about an hour to complete though does not require any recovery time after the procedure.

A radiologist performs IVP by injecting an iodine-based contrast medium into a VEIN in the arm. Some people experience a mild burning sensation with the contrast medium's injection. The person lies on the X-RAY table, and the radiologist takes X-rays at timed intervals as the contrast medium travels through the bloodstream and into the kidneys.

Sometimes the radiologist uses an inflatable compression belt, applied around the abdomen and back, to slow progress of the contrast medium through the kidneys. Near the end of the procedure the person urinates to empty the bladder, after which the radiologist takes a final series of X-rays.

It is important to drink plenty of water after an IVP to help flush the residual contrast medium from the body. Complications and side effects are rare, the most common being an allergic reaction to the contrast medium. People who have allergies to iodine or shellfish should discuss the possibility of sensitivity to the contrast medium with the radiologist or urologist before undergoing the IVP. The IVP provides an abundance of information about the structure and functions of the urinary system that is useful for the urologist in reaching or confirming diagnosis of numerous conditions affecting the kidneys.

See also COMPUTED TOMOGRAPHY (CT) SCAN; [CYS-TOURETHROGRAM](#).



Kegel exercises A series of exercises to strengthen the pubococcygeal muscle, a figure-eight double loop of **MUSCLE** that forms the pelvic floor. Arnold H. Kegel, MD, an American gynecologist who practiced in Los Angeles, California, popularized the pelvic muscle exercises that now bear his name when he developed a **BIOFEEDBACK** device called a perineometer in the 1940s. Though urologists and gynecologists had been instructing women in the procedure of these exercises for over a decade as treatment for **URINARY INCONTINENCE**, most women had no idea whether they were doing them correctly. The Kegel perineometer was the first device to measure the effectiveness of the cycles of contraction and relaxation of the pubococcygeal muscle. In conjunction with biofeedback, Kegel exercises became highly successful in resolving mild to moderate urinary incontinence in many women.

PERFORMING KEGEL EXERCISES

- Identify the pubococcygeal muscle by stopping and starting the flow of **URINATION** or, for women, inserting a finger into the **VAGINA**. Women or men may benefit from **BIOFEEDBACK** methods.
- Begin with 10 repetitions of the complete cycle of contract, hold, and relax. Maintain each stage for 10 seconds. Repeat three times a day.
- As pubococcygeal muscle **STRENGTH** improves, increase the length of each stage to 20 seconds and the number of repetitions gradually to 50. Repeat three times a day.

Kegel exercises, also called pelvic floor exercises, today remain the most effective noninvasive treatment for urinary incontinence in women—

and in men after surgery to treat **BENIGN PROSTATIC HYPERPLASIA (BPH)** or **PROSTATE CANCER**. Many obstetricians recommend Kegel exercises to speed recovery after **CHILDBIRTH**. Kegel exercises are also often helpful for treating premature **EJACULATION** in men. The exercises are very simple, consisting of cycles of contracting, holding, and relaxing the pubococcygeal muscle repeated several times a day. Once a person learns the exercises, he or she can perform them unnoticeably and when seated, standing, or lying down.

It is important to correctly identify the pubococcygeal muscle; the muscles of the buttocks, abdomen, and thighs should be relaxed when performing Kegel exercises. An easy way to learn to contract the pubococcygeal muscle is to consciously stop and start the flow of **URINE** when urinating. **BIOFEEDBACK** remains the most effective means for determining whether the person is performing the Kegel exercises correctly, and a variety of biofeedback devices are available for home use. Women may also use a simple device called a vaginal cone. Most people begin to experience results in about six to eight weeks. It is important to continue regularly with Kegel exercises to maintain optimal pubococcygeal muscle tone and **STRENGTH**.

See also [FECAL INCONTINENCE](#).

kidney cancer See [RENAL CANCER](#).

kidney cyst See [RENAL CYST](#).

kidney dialysis See [RENAL DIALYSIS](#).

kidney disease of diabetes See [NEPHROPATHY](#).

kidney donor An individual who donates his or her **KIDNEYS** after death or who donates one kidney

for live donor transplantation. Kidneys are the organs most commonly transplanted in the United States (other than SKIN and corneas). At present, people waiting for donor kidneys outnumber available kidneys nearly four to one. Between 50,000 and 60,000 people currently await donor kidneys in the United States. A person becomes a potential candidate for KIDNEY TRANSPLANTATION with the onset of END-STAGE RENAL DISEASE (ESRD), a permanent state of renal failure in which the kidneys cannot perform their functions at a level that sustains life.

The donor and the recipient must match in BLOOD TYPE and human leukocyte antigen factors and be negative for antibodies (negative cross-match). HUMAN LEUKOCYTE ANTIGENS (HLAS) are six inherited proteins (three from each parent) on the surfaces of leukocytes (white BLOOD cells). The more HLAs that match, the greater likelihood the recipient's body will accept the donor kidney. Even with blood type match and good HLA matching, some people's immune systems produce antibodies in reaction to the donor's blood. A negative crossmatch mixes small amounts of the prospective donor's blood and the recipient's blood to confirm that there is no ANTIBODY reaction.

Living Donor

A living donor may be a relative or a stranger to the kidney recipient. In general a living donor must be in overall good health and have two normally functioning kidneys. Some health conditions, such as HYPERTENSION (high BLOOD PRESSURE), chronic LIVER disease, and DIABETES, preclude a person from donating a kidney because the risk is high for developing kidney disease as a consequence of these conditions. People with chronic health conditions generally are not eligible to donate a kidney. There is no greater likelihood of developing kidney disease with only one kidney, and a single kidney can more than adequately accommodate the body's needs.

The transplant team selects a living donor on the basis of the match between the donor and the recipient. Typically, the recipient's health insurance pays for the donor's medical expenses related to the kidney donation, including surgery, hospitalization, and follow-up care. Once selected, the living donor undergoes NEPHRECTOMY, an OPERATION

to remove a kidney. There are two options, open nephrectomy and laparoscopic nephrectomy. Either procedure is a major surgery that requires hospitalization and postsurgical recovery time. Though recovery is uneventful for most donors whether they undergo laparoscopic or open nephrectomy, donating a kidney does require time off from work and regular activities.

Laparoscopic nephrectomy requires several small incisions through which the team uses laparoscopy to remove the donor kidney. Though technically more challenging for the transplant team, laparoscopic nephrectomy significantly reduces scarring and recovery time for the donor. Laparoscopic nephrectomy takes three to four hours, with two to three hours in the recovery room while the person returns to full consciousness. Most people who undergo laparoscopic nephrectomy stay one to three days in the hospital after the surgery and require four to six weeks for return to regular activities. Within a year or two, the small scars remaining from the incisions are nearly invisible.

Open nephrectomy requires a single large incision and takes two to three hours, with two to three hours in the recovery room to return to full consciousness. Most people who undergo open nephrectomy stay three to five days in the hospital after the surgery and need six to eight weeks for return to regular activities. The SCAR from the incision begins to fade in about a year.

The transplant team immediately performs the transplantation surgery to place the donor kidney into the recipient. Only the intended recipient may receive the living donor kidney; there are no waiting list requirements for live donor kidney transplantations. Living donor kidney transplants have a higher long-term success rate than cadaver donor kidney transplants.

Cadaver Donor

Cadaver donor kidneys come from the bodies of deceased persons who died of causes not related to kidney function, had healthy kidneys at the time of death, and signed documents affirming their desires to donate their organs after their deaths. Family members may make the decision about organ donation when the person dies without organ donor documentation. Organ donation can

proceed only when the appropriate assessments certify the person has suffered **BRAIN DEATH**.

UNIVERSAL DONOR CARD

Most states honor the universal donor card, a wallet-size document affirming a person's intent to donate his or her organs upon death, as a legal document. Many states incorporate the universal donor card into the driver's license.

A transplant team removes donor kidneys using sterile surgical technique and a procedure similar to nephrectomy (surgical removal of a kidney such as to treat **RENAL CANCER**), carefully preserving the blood vessels and **URETER**. After removing the kidneys, called organ harvesting, the transplant team places them in a cold solution that can sustain them for 36 to 48 hours and sutures closed the incisions made to gain access to the kidneys. The organ-processing procedure includes screening of the donor kidneys for any diseases they could convey to the recipient. In the United States an independent organization called the United Network for Organ Sharing (UNOS) oversees the collection and distribution of all cadaver donor organs in compliance with strict guidelines intended to ensure equity in the process of matching donor organs with recipients. The transplant surgery must take place within 36 to 48 hours of the kidney's harvesting, sooner if possible.

See also **ORGAN TRANSPLANTATION**; **QUALITY OF LIFE**; **SURGERY BENEFIT AND RISK ASSESSMENT**.

kidney failure See **RENAL FAILURE**.

kidneys A pair of organs responsible for filtering wastes and excess water from the **BLOOD**, excreting both from the body as **URINE**. The kidneys maintain the body's fluid and electrolyte balances, and also produce hormones that regulate the production of new erythrocytes (**ERYTHROPOIETIN [EPO]**) and **BLOOD PRESSURE (RENIN)**. With each heartbeat about 20 percent of the body's blood supply surges through the kidneys. The body's entire blood supply passes through the kidneys about two dozen times a day. Though the kidneys are essential for life, a single functioning kidney can adequately sustain life in most people. The kidneys are fully functional from birth.

Renal Structure

The kidneys are dark reddish brown in color, four to five inches long, and about two inches across. An adult kidney weighs five to six ounces, and is the same shape as the bean that bears its name. The kidneys rest against along the spinal column at the back of the abdominal cavity, one on each side of the **SPINAL CORD** and within the protective enclosure of the rib cage. The kidneys are retroperitoneal—that is, they lie outside the posterior layer of the peritoneum, the membrane that protects the abdominal structures. The left kidney is about an inch higher than the right. A cushion of fatty tissue surrounds each kidney, helping protect it as well as hold it in place. An adrenal gland resides atop each kidney though does not physically or functionally integrate with the kidney.

A thin but tough membrane called the renal capsule surrounds the kidney, helping contain and protect its blood-rich tissues. The outer layer of the kidney is the renal cortex and the inner layer the renal medulla. The renal **ARTERY**, renal **VEIN**, and **URETER** junction with the kidney where it indents, an area called the hilus. Deeper within the kidney at this junction is the renal pelvis, a deltalike region of the kidney that drains urine into the ureter. The functional unit of the kidney is the **NEPHRON**, a microscopic structure, a set of tubules that carry out the functions filtration, and a coil of capillaries, the **GLOMERULUS**, which brings in the blood for filtration. Each kidney contains over a million nephrons, each of which functions independently. The nephrons extend through the renal cortex and the renal medulla. The renal cortex contains the blood vessels that bring blood to the nephrons and the glomerulus for each nephron, as well as a portion of filtering tubule. The renal medulla consists of 8 to 12 wedge-shaped segments, called pyramids. The pyramids contain the filtering tubules, including the loop of Henle and the collecting tubule, for each nephron. Blood circulates primarily through the renal cortex, while the structures of the renal medulla direct water and waste products (urine) toward the renal pelvis and elimination via the ureter.

Renal Function

The pressure of the blood as it flows through the glomeruli helps force molecules of water and

other substances across the membranous glomerular walls and into an encapsulated structure called Bowman’s capsule. Specialized proteins called transporters carry these substances across the capillary membranes. The collected mixture, called filtrate, funnels from the Bowman’s capsule into the tubules. A separate capillary network, the peritubular capillaries, entwines the filtration tubules to allow water and other substances to return to the blood circulation (reabsorption). By the time a heartbeat’s surge of blood completes its passage through the nephrons, about 99 percent of the water and electrolytes originally filtered from the blood (sodium, potassium, magnesium, calcium, and others) have returned to the circulation.

Kidney function remains at a fairly constant level for much of life. By the 40s, the kidneys begin to lose nephrons at a rate of about 10 percent per decade. As a single kidney can meet the body’s needs having only about one third of its capacity, the kidneys are well structured to function the length of the lifespan. The primary threats to kidney function are diseases that affect other body systems or the body as a whole, such as **DIA-BETES**, **HYPERTENSION** (high blood pressure), and **CARDIOVASCULAR DISEASE (CVD)**.

The kidneys also produce two vital hormones: **RENIN**, which controls blood pressure, and **EPO**, which regulates erythropoiesis (the synthesis of new erythrocytes in the **BONE MARROW**). Health conditions that damage the kidneys also affect their ability to produce these hormones. Interstitial cells (cells in the body of the kidney) produce both hormones.

The pressure of blood flowing through the glomeruli helps determine whether the kidney releases renin, which is a process of perpetual balance. Renin sets in motion the cascade of events through which the body produces angiotensin II, a potent vasoconstrictor (chemical that narrows and stiffens the blood vessels to raise blood pressure). The kidneys also respond to the release of **ANTIDI-URETIC HORMONE (ADH)** from the **HYPOTHALAMUS**, another mechanism of blood pressure regulation that influences the amount of water the kidneys withhold in the blood or excrete in the urine. The hypothalamus releases ADH to cause the kidneys to withhold more water, which increases the blood volume and thus the blood pressure.

The kidneys also detect the level of erythrocytes that are in the blood as it passes through them, and release erythropoietin when the erythrocyte level drops. Erythropoietin stimulates the production of reticulocytes in the bone marrow and their release into the blood circulation, where they mature to become oxygen-bearing erythrocytes.

HEALTH CONDITIONS THAT AFFECT THE KIDNEYS

ALPURT’S SYNDROME	END-STAGE RENAL DISEASE (ESRD)
GLOMERULONEPHRITIS	GLOMERULOSCLEROSIS
GOODPASTURE’S SYNDROME	HEMOLYTIC UREMIC SYNDROME
HEPATORENAL FAILURE	HORSESHOE KIDNEY
HYDRONEPHROSIS	kidney cyst
MINIMAL CHANGE DISEASE	NEPHRITIS
NEPHROLITHIASIS	NEPHROPATHY of DIABETES
nephropathy of HYPERTENSION	NEPHROTIC SYNDROME
POLYCYSTIC KIDNEY DISEASE	pyelonephritis
RENAL CANCER	RENAL FAILURE
renal osteodystrophy	RENAL TUBULAR ACIDOSIS
rhabdomyolysis	WILMS’S TUMOR

For further discussion of the kidneys within the context of the urinary system’s structure and function please see the overview section “The Urinary System.”

See also **BLADDER**; **ERYTHROCYTE**; **HEMATOPOIESIS**; **HORSESHOE KIDNEY**; **RETICULOCYTE**; **URETHRA**.

kidney stone See **NEPHROLITHIASIS**.

kidney transplantation A surgical OPERATION to place a healthy, functioning kidney into a person whose own kidneys have permanently failed. The first successful kidney transplantation took place between identical twin brothers in 1954. However, until the discovery of the immunosuppressive **DRUG** cyclosporine in 1983, the risk of organ rejection was very high, and kidney transplantation was a treatment of last resort. With current **IMMUNOSUPPRESSIVE THERAPY** the recipient of a transplanted kidney can expect to live 5 to 20 years or longer with relatively normal kidney function.

Since the mid-1980s kidney transplantation has become the standard of treatment for **END-STAGE RENAL DISEASE (ESRD)**, also called permanent kidney failure (**RENAL FAILURE**). Transplant surgeons in the United States perform about 15,000 kidney transplant operations each year. However, a severe

shortage of donor kidneys limits the availability of kidney transplantation. Another 30,000 to 45,000 people are eligible for kidney transplantations and await donor organs. A donor kidney may be a cadaver organ donation (donated after a person's death) or come from a person who has two healthy kidneys and offers to donate one to the recipient.

In the United States, the federal health-care program Medicare pays for 80 percent of most expenses related to kidney transplantation for those who meet the qualification criteria. The U.S. Centers for Medicare and Medicaid Services Web site (www.cms.hhs.gov) provides comprehensive information about eligibility and covered services. Private health insurance and other public programs also provide coverage for kidney transplantation costs, though coverage varies among carriers and programs.

Donor Kidneys

The primary source of donor kidneys is cadaver donation—people who authorize the donation of their organs when they die. In the United States the United Network for Organ Sharing (UNOS) administers the nationwide cadaver donor organ collection and distribution program, the Organ Procurement and Transplantation Network (OPTN). People eligible for kidney transplantation register with OPTN through regional organ transplantation centers. OPTN follows strict guidelines intended to ensure equitable access to donor organs. People may wait several months to several years for a matched cadaver donor kidney, as the OPTN system distributes organs to matched recipients who are the sickest.

The wait time for a living donor kidney transplant is typically significantly shorter, often only several months, because as soon as the transplant team confirms the intended donor is a match the surgeries (donation and transplantation) can take place. Living organ donation does not fall within OPTN. Only the intended recipient may receive the kidney from the living donor. The living donor is often a family member though may be a stranger who is a strong match with the recipient.

Donor-Recipient Match

The donor kidney must match the recipient as closely as possible in three ways. First, the donor

and the recipient must have the same BLOOD TYPE. Second, the donor and the recipient must match HUMAN LEUKOCYTE ANTIGENS (HLAs), which are proteins on the surfaces of leukocytes (white BLOOD cells), as closely as possible. Every person has six HLAs. The more HLAs that match between donor and recipient, the higher the likelihood that the recipient's body will accept the donor kidney (though all organ transplant recipients take lifelong immunosuppressive therapy). Transplant surgeons like to see a match of three or more HLAs. Third, the donor's blood must not initiate an ANTIBODY response with the recipient's blood (called a negative crossmatch), which the transplant team tests by mixing samples of blood from each in a test tube.

Surgical Procedure

The transplant surgery generally takes three to five hours. With the person under general ANESTHESIA, the transplant surgeon makes an incision in the lower abdomen, placing the donor kidney in the abdominal cavity below the native kidneys. The surgeon attaches the donor kidney's arteries and veins to the recipient's iliac ARTERY and iliac VEIN, respectively, and the donor kidney's URETER to the BLADDER. Depending on the reason for the ESRD, the surgeon may either leave or remove the recipient's nonfunctioning kidneys. After returning to full consciousness in the recovery room, the recipient typically remains in the hospital for three to five days. The transplanted kidney may begin functioning immediately or take several weeks. The recipient undergoes RENAL DIALYSIS until kidney function becomes adequate.

Risks and Complications

The risks of transplantation surgery include bleeding during or after the operation and postoperative INFECTION. Because the transplanted kidney is lower in the abdomen than the native kidneys it lacks the protection of the rib cage and is more vulnerable to traumatic injury. Rarely the recipient's body may immediately reject the donor organ, in which case the transplant team must operate again to remove it. Most people recover fully from the surgery without complications, though there is always the risk of organ rejection. Many kidney transplant recipients experience episodes of organ rejection that the transplant

doctor can treat with various medications. The IMMUNOSUPPRESSIVE THERAPY that is necessary for organ transplant recipients to take lowers the body's overall immune response, lowering resistance to infection. IMMUNOSUPPRESSIVE MEDICATIONS have numerous other side effects as well. People who take long-term immunosuppressive therapy do have an increased risk for LYMPHOMA, a type of cancer that affects the lymph nodes.

Outlook and Lifestyle Modifications

Most people who receive transplanted kidneys feel better immediately after surgery and enjoy rela-

tively normal lifestyles after recovering from surgery; however, they must continue taking immunosuppressive medications and receive regular medical checkups to monitor the health of their transplanted kidneys. Doctors generally recommend that people who have transplanted kidneys avoid activities with increased risk for blunt trauma to the abdomen, such as contact sports. The doctor may further recommend specific dietary and lifestyle modifications to maintain optimal kidney function.

See also ORGAN TRANSPLANTATION; SURGERY BENEFIT AND RISK ASSESSMENT.



Medicare coverage for permanent renal failure

Federal government funding in the United States that pays for medical treatment for people of any age who have **END-STAGE RENAL DISEASE (ESRD)**, also called **permanent RENAL FAILURE**. Though for other health conditions an individual must be age 65 or older to qualify for Medicare coverage, the US Congress in 1973 passed legislation broadening Medicare coverage to include care for ESRD at any age. There are specific eligibility requirements and co-payments. Health-care providers that offer care for ESRD have information about the application and approval processes. The US Centers for Medicare and Medicaid Services Web site (www.cms.hhs.gov) also provides comprehensive information about eligibility and covered services.

See also [KIDNEY TRANSPLANTATION](#); [QUALITY OF LIFE](#); [RENAL DIALYSIS](#).

micturition See [URINATION](#).

minimal change disease A disorder of kidney function in which the structure of the **KIDNEYS**, notably the nephrons, appears normal with regular (light) microscope examination though slightly abnormal with electron microscope examination. Minimal change disease is primarily a condition of childhood (usually in children under age six) and seldom occurs in adults. Researchers believe the condition is one of immune dysfunction in which T-cell lymphocytes cause molecular damage to the delicate walls of the glomeruli. The damage allows **ALBUMIN** (protein) to leak from the **BLOOD** into the **URINE** (**ALBUMINURIA**).

Symptoms and Diagnostic Path

The symptoms of minimal change disease are often vague and include

- edema, often of the face
- fatigue
- **MUSCLE**-wasting
- impaired growth
- unexplained weight gain

The diagnostic path begins with urinalysis, which typically shows albuminuria (albumin excretion). Other laboratory tests are often normal. There is a high correlation between minimal change disease and **NEPHROTIC SYNDROME**, a constellation of symptoms that indicate kidney dysfunction. The urologist may recommend a trial of treatment before conducting further, more invasive diagnostic procedures.

Treatment Options and Outlook

Treatment for minimal change disease is **IMMUNOSUPPRESSIVE THERAPY** with **CORTICOSTEROID MEDICATIONS** such as prednisone. Most children improve remarkably within two weeks, and nearly all within six to eight weeks. The nephrologist may make dietary recommendations to maintain appropriate protein, sodium, and fluid intake. Minimal change disease fully resolves, without residual damage to the kidneys, with treatment in most children. About 10 percent of children experience periodic **RECURRENCE** of symptoms through **ADOLESCENCE** and sometimes into adulthood. Children taking corticosteroid medications have a somewhat increased risk for **INFECTION** during the course of therapy.

Risk Factors and Preventive Measures

Because researchers do not know what causes minimal change disease, there are no measures to prevent its occurrence. Prompt treatment mini-

mizes the risk for permanent damage to the kidneys.

See also [GLOMERULONEPHRITIS](#); [GLOMERULOSCLEROSIS](#); [NEPHRON](#).

nephrectomy A surgical OPERATION to remove a kidney. The most common reasons for nephrectomy are to treat RENAL CANCER, to remove a kidney for live donor KIDNEY TRANSPLANTATION, and to remove a kidney that is severely injured due to trauma or malformed due to CONGENITAL ANOMALY. There are three kinds of nephrectomy:

- partial nephrectomy, in which the surgeon removes only a portion of the kidney
- simple nephrectomy, in which the surgeon removes the entire kidney though leaves the surrounding tissue intact
- radical nephrectomy, in which the surgeon removes the kidney, surrounding tissues, and adjacent lymph nodes

Nephrectomy may be an open surgery, in which the surgeon operates through a large incision in the flank (side of the back), or laparoscopic, in which the surgeon operates through multiple small incisions using a laparoscope.

Surgical Procedure

Nephrectomy takes place in a hospital operating room with the person under general ANESTHESIA. For open nephrectomy, the surgeon makes a large incision into the flank over the kidney. The incision gives access to the kidney without the need to penetrate the peritoneum, as the KIDNEYS lie behind this protective membrane. The surgeon sutures off the renal ARTERY and VEIN and the URETER, then carefully cuts the kidney away from the adipose tissue that surrounds it and holds it in place. When the operation is radical nephrectomy for renal cancer, the surgeon also removes the adipose tissue, nearby connective tissue, and adjacent lymph nodes. After removing the kidney the surgeon sutures closed the incision, which will heal into a SCAR. Open nephrectomy takes two to four hours.

For laparoscopic nephrectomy, also called minimally invasive nephrectomy, the surgeon makes four or five small incisions, called ports, in locations around the flank on the side where the kid-

ney will be removed. The surgeon inserts the laparoscope through one of the ports, and uses another to inflate the interior of the abdomen with a gas. The surgeon inserts instruments through the remaining ports. The laparoscope has a light and camera on the tip that conveys the image of the interior abdomen to a closed-circuit television monitor. The surgeon operates by watching the monitor. When the kidney is free from its BLOOD supply and connecting tissues, the surgeon inserts a special bag through one of the ports and puts the kidney into it. The surgeon carefully delivers the bag through the port, enlarging the port if necessary. When the kidney is out, the surgeon removes the instruments and laparoscope from their ports and sutures them closed. The ports heal into small scars. Laparoscopic nephrectomy takes three to five hours.

After either type of surgery, the person remains in the recovery room until fully awakened from the anesthesia and then goes to a hospital room. The hospital stay for open nephrectomy is generally five to seven days and for laparoscopic nephrectomy is generally three to five days. A person who undergoes open nephrectomy typically returns to regular activities in 8 to 12 weeks. A person who undergoes laparoscopic nephrectomy typically returns to regular activities in five to six weeks.

Risks and Complications

The primary risks of nephrectomy are bleeding and INFECTION, along with the potential for complications arising from anesthesia. These are uncommon events. The doctor will prescribe ANALGESIC MEDICATIONS to relieve postoperative PAIN. Further risks depend on the reasons for the nephrectomy. Some people experience fluctuations in BLOOD PRESSURE during the first few days after the nephrectomy, as the kidneys are key to regulating blood pressure in the body. This nearly always stabilizes without the need for treatment.

Outlook and Lifestyle Modifications

Most people fully recover and return to their regular activities after nephrectomy. The remaining kidney, if healthy, can more than adequately sustain the body's needs. People who have renal cancer often undergo follow-up CHEMOTHERAPY OR RADIA-

TION THERAPY after surgery. The doctor may recommend dietary changes and other lifestyle modifications, depending on the person's general health status. A single kidney provides more than adequate function for people who are otherwise in reasonably good health. Lifestyle factors such as nutritious EATING HABITS, daily physical exercise, and maintaining healthy weight reduce strain on the kidney as well as the risk for HYPERTENSION (high blood pressure) and DIABETES, the two health conditions that are most likely to cause kidney disease.

See also MINIMALLY INVASIVE SURGERY; POSTOPERATIVE PROCEDURES; PREOPERATIVE PROCEDURES; SURGERY BENEFIT AND RISK ASSESSMENT.

nephritis INFLAMMATION of the kidney. The most common causes of nephritis are bacterial INFECTION, which generally cause acute (sudden onset) nephritis, and AUTOIMMUNE DISORDERS, which tend to cause chronic or recurrent inflammation. Nephritis can be acute (come on suddenly), chronic (long-term), or recurrent (repeated episodes of acute nephritis). Chronic nephritis can lead to NEPHROPATHY.

Bacterial nephritis When infection involves the glomeruli, it is infectious GLOMERULONEPHRITIS. Infectious glomerulonephritis develops as a complication of untreated or undertreated STREP THROAT or other streptococcal infection elsewhere in the body. Occasionally another bacterial strain such as staphylococcus is responsible. Infection that travels up the ureters from the BLADDER as a complication of untreated or undertreated URINARY TRACT INFECTION (UTI) is pyelonephritis. In pyelonephritis the infection involves the pelvis of the kidney where URINE drains from the kidney into the ureters. VESICoureTERAL REFLUX, in which urine backflows from the bladder through the ureters to the kidneys, is a common cause of pyelonephritis.

Interstitial nephritis In interstitial nephritis the inflammation affects the spaces between the tubules in the nephrons. Such inflammation is nearly always a consequence of acute toxic nephropathy. Medications such as penicillin and penicillin-derived antibiotics, the diuretic medication furosemide and thiazide diuretics, and NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) are commonly responsible for acute interstitial nephritis. The nephritis generally resolves without

lingering complications within a few weeks of stopping the medication.

Lupus nephritis The autoimmune disorder SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) affects the KIDNEYS in about 40 percent of people who have SLE. In some people, lupus nephritis may be the only manifestation of SLE. Lupus nephritis can progress rapidly to RENAL FAILURE and END-STAGE RENAL DISEASE (ESRD). Because women who have SLE outnumber men who have SLE nearly nine to one, lupus nephritis far more commonly affects women.

Hereditary nephritis Hereditary nephritis is a genetic disorder that results from GENE mutations. The symptoms of hereditary nephritis are apparent at or shortly after birth, and the inflammation tends to be progressive. The most frequent presentation of hereditary nephritis is ALPORT'S SYNDROME, a disorder of protein encoding.

Symptoms and Diagnostic Path

The symptoms of nephritis may include

- HEMATURIA (bloody urine)
- OLIGURIA (diminished urine volume)
- edema (fluid retention that causes swelling in the tissues), notably of the face, hands and arms, and legs and feet
- loss of APPETITE, NAUSEA, and VOMITING
- FEVER (bacterial nephritis)

The diagnostic path begins with urinalysis and BLOOD tests that assess kidney function. Urinalysis may show the presence of BACTERIA, indicating the cause of the nephritis is infection. Other diagnostic procedures the nephrologist may choose to conduct include further blood and urine tests, ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, and kidney biopsy. The biopsy shows the presence of inflammation and any damage that has occurred to the tubules or glomeruli.

Treatment Options and Outlook

Treatment depends on the underlying cause. Bacterial nephritis requires antibiotic therapy, often long term (up to six months). Severe infection requires hospitalization for intravenous ANTIBIOTIC MEDICATIONS. Most people recover fully and without residual damage from bacterial nephritis.

Because the kidneys play key roles in regulating BLOOD PRESSURE kidney disease that interferes with such functions can result in HYPERTENSION (high blood pressure), which requires treatment. The doctor may recommend dietary changes to limit sodium, protein, and water intake. Treatment for lupus nephritis often includes IMMUNOSUPPRESSIVE THERAPY.

Risk Factors and Preventive Measures

The primary risk factors for nephritis are the conditions that can cause it. Nephrotoxins are generally avoidable once the doctor identifies them as responsible for the nephritis. Bacterial infections nearly always migrate to the kidneys from elsewhere in the body. Early and appropriate treatment for the primary infection, particularly strep throat, helps prevent the infection from spreading to the kidneys.

See also [GLOMERULONEPHRITIS](#); [GLOMERULOSCLEROSIS](#); [INHERITANCE PATTERNS](#); [NEPHROPATHY](#); [NEPHROTIC SYNDROME](#).

nephrolithiasis The formation of calcifications (also called calculi) in the KIDNEYS, usually called kidney stones. Kidney stones are common, with about 1 in 10 adults in the United States likely to have at least one over the course of adulthood. Some people pass kidney stones with little discomfort and may not even be aware of them, though for many people nephrolithiasis is extremely painful and debilitating. Kidney stones may lodge in the ureters or within the kidney, usually in the renal pelvis or a structure within the renal medulla called the calyx where the collection tubules empty their URINE.

Kidney stones that block the flow of URINE constitute a medical emergency that may require immediate treatment.

About 75 percent of kidney stones are made of calcium in combination with oxalate, phosphate, or carbonate. Calcium oxalate stones are the most common. About 10 percent of stones are made of uric acid and occur most frequently in men who have GOUT (a form of arthritis) or in people who are undergoing CHEMOTHERAPY. Other stones may form of cystine, an amino acid compound, or of

struvite, a compound of magnesium, ammonia, and phosphate that tends to form in women who have frequent bacterial urinary tract infections (UTIs).

Symptoms and Diagnostic Path

Common symptoms of kidney stones include

- rapid onset of excruciating PAIN in the side (flank) or back
- persistent or colicky (wavelike) ABDOMINAL PAIN
- NAUSEA and VOMITING
- URINARY FREQUENCY and URINARY URGENCY
- FEVER and chills
- NOCTURIA (urination at night)
- groin pain in men or women or testicular pain in men

The diagnostic path may include abdominal X-RAY, ULTRASOUND, OR COMPUTED TOMOGRAPHY (CT) SCAN to detect the location of the stone. The doctor may also choose to conduct an INTRAVENOUS PYELOGRAM (IVP) to assess the extent to which a stone is blocking the flow of BLOOD or urine. Blood and urine tests may show elevated levels of calcium, uric acid, or oxalate.

Treatment Options and Outlook

Treatment for nephrolithiasis with severe pain begins with analgesic medication, often narcotic, to relieve the pain. Further treatment to move the stone out of the urinary tract may include EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY (ESWL), a noninvasive method that effectively disperses stones up to 2 centimeters in diameter, or surgery such as percutaneous lithotomy in which the nephrologist uses laparoscopic surgery to snare and remove the stone. Most urologists prefer to take a course of watchful waiting with calculi that are not causing symptoms or that appear small enough to be able to pass through the urinary tract on their own, often recommending increased water consumption to increase the volume of the urine.

Kidney stones tend to recur, so often it is useful to determine the stone's composition, as this helps the nephrologist or urologist assess appropriate measures to reduce the risk for future stone formation. The doctor will likely recommend strain-

ing the urine to capture the stones or stone fragments when they pass, for laboratory analysis. Despite the pain they cause, kidney stones do not usually cause permanent damage to the kidneys.

People who have had kidney stones should make dietary modifications, such as calcium restriction, only if the doctor specifically recommends them. Though doctors once believed dietary calcium was a key culprit in the development of kidney stones, recent research shows that when blood levels of calcium are too high (**HYPERCALCEMIA**) the cause is more likely to be overabsorption from the gastrointestinal tract than excessive consumption. Cutting back on dietary calcium in such a situation can have the opposite and undesired consequence of increasing gastrointestinal absorption of calcium. Dietary calcium is essential for **BONE STRENGTH** and health, tissue **HEALING**, and proper **NERVE** and **MUSCLE** function.

Risk Factors and Preventive Measures

Men are more likely than women to develop kidney stones. As well, kidney stones appear to run in families, suggesting a genetic or hereditary component. People who have **RENAL TUBULAR ACIDOSIS** or **INFLAMMATORY BOWEL DISEASE (IBD)** have increased risk for developing nephrolithiasis. Lifestyle measures to reduce the risk for kidney stones include drinking six to eight 8-ounce glasses of water and getting physical exercise daily. These measures increase the volume of urine, helping dissolve minerals that might crystallize, and keeps the urine moving through the urinary system. The doctor may prescribe medication to reduce the risk of kidney stones in people who have history of **RECURRENCE**.

See also **CYSTINURIA**; **HYPEROXALURIA**; **MINIMALLY INVASIVE SURGERY**; **URINARY TRACT INFECTION (UTI)**; **UROLITHIASIS**.

nephron The microscopic functional unit of the kidney. Each kidney contains more than a million nephrons, each of which extends from the renal cortex into the renal medulla in fairly linear fashion. Two elements make up the nephron: the renal tubules and the renal corpuscle. The renal corpuscle contains the **GLOMERULUS**, the coiled network of capillaries that bring **BLOOD** into the nephron, and Bowman's capsule, the podlike structure that

encases the glomerulus. The pressure of the blood as it enters the glomerulus forces molecules of water, electrolytes, and other substances through the thin glomerular wall into Bowman's capsule. This mixture, called filtrate, collects in the capsule and drains into the renal tubule. Each segment of the tubule reabsorbs different substances from the filtrate as it passes through them. A second network of capillaries separate from the glomerulus, the peritubular capillaries, entwines the renal tubule to allow the reabsorbed materials to reenter the blood circulation.

The first portion of the tubule to exit Bowman's capsule, the proximal tubule (also called the proximal convoluted tubule), runs along the renal corpuscle, heading inward toward the renal medulla though it remains within the renal cortex. The proximal tubule reabsorbs about two thirds of the sodium and two thirds of the water the filtrate contains, and reabsorbs calcium when vitamin D is present. The next segment, the loop of Henle, drops deep into the renal medulla, makes a sharp loop, and rises back up into the renal cortex in somewhat of a hairpin appearance. Different portions of the loop of Henle reabsorb sodium, potassium, chloride, magnesium, calcium, and water. The loop of Henle plays a significant role in the concentration and dilution of the **URINE**, and is the target of some types of diuretic medications. The distal tubule (also called the distal convoluted tubule) continues up through the renal cortex and wraps around the renal corpuscle, ultimately joining with the collecting tubule (also called the collecting duct). The distal tubule reabsorbs sodium and bicarbonate and secretes potassium. The final segment of the renal tubule is the collecting tubule, which funnels the remaining filtrate toward the renal pelvis for excretion via the **URETER** as urine. Only water reabsorption takes place from the collecting tubule.

For further discussion of the nephron within the context of the urinary system's structure and function please see the overview section "The Urinary System."

See also **BLADDER**; **FANCONI'S SYNDROME**; **KIDNEYS**; **URETHRA**.

nephropathy Progressive, irreversible damage to the **KIDNEYS** that occurs as a result of systemic

health conditions or disease processes. Nephropathy is the main cause of END-STAGE RENAL DISEASE (ESRD) and the leading reason for KIDNEY TRANSPLANTATION. Doctors diagnose more than 100,000 Americans with nephropathy every year. DIABETES and HYPERTENSION (high BLOOD PRESSURE) are the leading cause of nephropathy in the United States. These conditions damage the delicate glomeruli, the capillary networks that feed BLOOD through the nephrons, the filtering structures of the kidneys. Each kidney contains more than a million nephrons and can tolerate the loss of about two thirds of them before symptoms of kidney failure become apparent. By such time, however, damage to the kidneys is usually profound.

Nephropathy of diabetes Diabetes accounts for 45 percent of kidney failure among Americans. The elevated GLUCOSE (sugar) levels in the blood that occur with diabetes are particularly damaging to the blood vessels and the nerves that serve them. For reasons researchers do not understand, African Americans, Hispanic Americans, and Native Americans who have diabetes are significantly more likely to develop nephropathy of diabetes (sometimes called diabetic nephropathy). About 40 percent of people who have diabetes develop some degree of nephropathy, half of whom eventually progress to ESRD. Nephropathy is more likely in type 1 diabetes.

Nephropathy of hypertension Hypertension accounts for 25 percent of nephropathy among Americans. Chronically elevated blood pressure places considerable stress against the walls of the glomeruli, causing microscopic ruptures and scarring (fibrosis). As with nephropathy of diabetes, nephropathy of hypertension (sometimes called hypertensive nephropathy) is significantly more likely to develop in African Americans, Hispanic Americans, and Native Americans. The progression to ESRD can be rapid in poorly controlled or untreated hypertension.

IgA nephropathy In IMMUNOGLOBULIN A (IgA) nephropathy, a dysfunction of the IMMUNE SYSTEM results in deposits of gA, a protein, accumulating within the tubules of the nephrons. The kidneys have no process for removing these deposits, which eventually clog the tubules and prevent them from transporting filtrate. IgA nephropathy typically is ongoing for 20 years or longer before

causing enough damage to result in symptoms. Many people who have IgA nephropathy also have a systemic autoimmune disorder such as SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), RHEUMATOID ARTHRITIS, or ANKYLOSING SPONDYLITIS. Treating the underlying autoimmune disorder often slows the progression of the nephropathy.

Toxic nephropathy Many drugs and chemicals are nephrotoxins, substances that damage the kidneys. Toxic nephropathy typically develops as a result of chronic exposure though can occur with limited though substantial exposure (such as DRUG overdose). Common nephrotoxins include heavy metals (such as lead and cadmium), organic solvents (such as benzene), and certain ANTIBIOTIC MEDICATIONS (notably gentamicin and streptomycin, which are sometimes the only antibiotics effective against life-threatening infections such as bacterial MENINGITIS).

Worrisome culprits are the NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS). DEHYDRATION in combination with NSAID use, which occurs among people who compete in ENDURANCE activities, is a particular risk. Long-term, daily use of other pain-relief medications, notably codeine and combination products that contain CAFFEINE with acetaminophen or aspirin, also can cause this form of toxic nephropathy, commonly called analgesic nephropathy. People who have conditions of chronic PAIN are most susceptible to analgesic nephropathy. People who have diabetes or congestive HEART FAILURE, have other kidney disease, engage in heavy ALCOHOL consumption, or are age 70 or older also have increased risk for analgesic nephropathy, in part because many people do not understand the danger regular analgesic use poses for the kidneys. These circumstances reduce kidney function, increasing the likelihood that further damage to the kidneys will result in kidney failure.

Symptoms and Diagnostic Path

Nephropathy generally does not show symptoms until damage to the kidneys is fairly advanced. One of the earliest indications of nephropathy is ALBUMINURIA, a consequence of protein leaking from the glomeruli into the filtrate. Doctors often detect albuminuria through urinalysis done as part of a routine medical examination. When symptoms do appear, they often include

- frothy URINE during URINATION (indicates albuminuria)
- edema (fluid accumulation in the tissues), most noticeable upon awakening and often affecting the face and the feet
- fatigue
- loss of APPETITE in combination with increased weight (weight gain results from edema)
- HEADACHE

Some forms of nephropathy also cause painless HEMATURIA (bloody urine). The diagnostic path includes further urine tests as well as BLOOD tests to assess kidney function. The nephrologist may perform a kidney biopsy to examine the nephrons under the microscope, which reveals the microscopic damage of nephropathy. The nephrologist may also conduct diagnostic imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN and INTRAVENOUS PYELOGRAM (IVP) to examine kidney structure and function.

Treatment Options and Outlook

Treatment targets the underlying condition with the aim of slowing progression of the nephropathy and preserving remaining kidney function. It is critically important for people who have diabetes or hypertension (or both) to maintain effective control of these conditions through medication therapy and lifestyle measures. Some people are able to successfully manage the underlying condition and the nephropathy to avoid ESRD, though often nephropathy progresses to require RENAL DIALYSIS. Whether kidney transplantation is a viable treatment option for ESRD resulting from nephropathy depends on multiple factors, including co-existing health conditions, age, and overall health status.

Risk Factors and Preventive Measures

Diabetes and hypertension combined cause more two thirds of nephropathy in the United States. The risk for nephropathy is particularly high for people who have both these conditions. Preventing these conditions and appropriately and diligently treating them when they develop mitigates the risk for nephropathy. People who take long-term NSAIDs to treat chronic conditions such as

OSTEOARTHRITIS should have regular blood and urine tests to screen for early indications of nephropathy, and work with their doctors to find the lowest effective DOSE and least nephrotoxic medication to manage the condition and its symptoms.

See also HEAVY-METAL POISONING; HEPATORENAL FAILURE; NEPHRITIS; NEPHRON; NEPHROTIC SYNDROME; RETINOPATHY.

nephrotic syndrome A constellation of symptoms that result as a consequence of conditions that damage the glomeruli within the renal nephrons. The damage allows excessive protein to move through the walls of the glomeruli into the filtrate. The tubules are unable to reabsorb the large protein molecules, so the body ends up excreting the protein in the URINE (ALBUMINURIA). The excessive excretion of protein results in HYPOALBUMINEMIA, or low levels of ALBUMIN in the BLOOD circulation. The hypoalbuminemia allows fluid to leave the blood circulation and enter the interstitial tissues, where it accumulates to cause edema (swelling). Because the blood volume is now low, the KIDNEYS compensate by reabsorbing higher levels of water and sodium.

Most people who have nephrotic syndrome have diagnosed kidney disease so the underlying cause is clear. When indications of nephrotic syndrome occur in someone who does not have kidney disease, the diagnostic path begins with blood and urine tests to assess kidney function. Further diagnostic procedures then strive to identify the underlying renal condition. Treatment targets the underlying renal condition as well as symptoms such as HYPERTENSION (high BLOOD PRESSURE) and RENAL FAILURE. Treatment may include RENAL DIALYSIS when renal function is significantly impaired. The outlook depends on the underlying renal condition and its response to treatment. Symptoms of nephrotic syndrome generally resolve when the underlying condition improves.

See also GLOMERULONEPHRITIS; GLOMERULOSCLEROSIS; MINIMAL CHANGE DISEASE; NEPHRITIS; NEPHRON; UREMIA.

nephrotoxins Substances such as medications or environmental chemicals that damage the glomeruli and the tubules within the nephrons of

the KIDNEYS. Among those most commonly associated with altered kidney function and RENAL FAILURE are

- heavy metals such as lead, mercury, cadmium, and arsenic; exposure to these metals is most often occupational
- NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) such as ibuprofen, naproxen, and ketoprofen
- possibly acetaminophen
- Contrast dyes used in radiologic procedures
- certain ANTIBIOTIC MEDICATIONS, notably streptomycin and gentamicin
- organic solvents such as benzene

People who already have compromised kidney function or conditions such as DIABETES or HYPERTENSION (high BLOOD PRESSURE) are at greater risk for kidney damage resulting from nephrotoxins. Chronic DEHYDRATION, such as may occur with diuretic therapy or insufficient water consumption, increases the risk for kidney damage resulting from medications, especially NSAIDs.

See also [HEPATOTOXINS](#); [NEPHRON](#); [NEPHROPATHY](#).

neurogenic bladder A condition in which the nerves that control the BLADDER do not work properly, allowing the bladder to be underactive (hypotonic) or overactive (spastic). Damage may occur to the SPINAL CORD AND SPINAL NERVES, BRAIN, or PERIPHERAL NERVES that serve the bladder. Conditions that can cause such damage include traumatic injury, STROKE, degenerative neurologic disorders such as MULTIPLE SCLEROSIS and PARKINSON’S DISEASE, NEUROPATHY of DIABETES and neuropathy of HIV/AIDS, and injury to the nerves of the bladder as a consequence of pelvic surgery (such as PROSTATECTOMY in men or HYSTERECTOMY in women). URINARY INCONTINENCE is the most common consequence of neurogenic bladder.

The diagnostic path includes urinalysis, BLOOD tests, and diagnostic imaging procedures such as CYSTOSCOPY, ULTRASOUND, or COMPUTED TOMOGRAPHY (CT) SCAN. The urologist may also perform a voiding CYSTOURETHROGRAM to evaluate the flow of URINE through the urinary system. Electromyogram (EMG) measures the response of the nerves

and muscles of the bladder and urethra to mild electrical stimuli. Other tests can measure the capacity and rate of emptying of the bladder.

Treatment targets the underlying cause of the neurogenic bladder when possible. Other treatment measures aim to improve urinary incontinence. The success of the treatment often depends on the underlying cause. Various medications may increase or decrease the bladder’s responses. Surgery is sometimes an option. Though it may take time and much trial and error, most people find acceptable measures for accommodating neurogenic bladder.

See also [SPINAL CORD INJURY](#); [TRAUMATIC BRAIN INJURY \(TBI\)](#); [URINARY TRACT INFECTION \(UTI\)](#).

nocturia The need to get up from nighttime sleep to urinate. Nocturia is a significant cause of SLEEP DISORDERS though has numerous potential causes. Nocturia becomes more common with increasing age in both women and men, sometimes simply as a consequence of normal age-related changes that occur in the urinary tract. Key among these changes is the reduced ability of the BLADDER to distend because lost elasticity in the tissues, effectively shrinking the bladder’s capacity.

Many people are unaware how much fluid they drink in the evening. The urinary system is still processing all this fluid when the person lies down to go to bed. Often, simply changing habits to minimize fluid consumption after dinner is enough to slow URINE production through the night. When nocturia persists despite such measures, the urologist may prescribe medications such as tolterodine or oxybutynin that slow the bladder’s response.

**CONDITIONS FOR WHICH
NOCTURIA IS A COMMON SYMPTOM**

BENIGN PROSTATIC HYPERPLASIA (BPH)	CYSTITIS
CYSTOCELE	HYDRONEPHROSIS
NEPHROLITHIASIS	NEUROGENIC BLADDER
PROSTATITIS	URINARY TRACT INFECTION (UTI)
UROLITHIASIS	VAGINITIS

See also [AGING](#), [URINARY SYSTEM CHANGES THAT OCCUR WITH](#); [ENURESIS](#); [URINARY INCONTINENCE](#).

oliguria Significantly reduced URINE production that occurs as a consequence of RENAL FAILURE, DEHYDRATION, hemorrhage (massive BLOOD loss), or SHOCK. Normal adult urinary output is 1500 milliliters to 3000 milliliters per day. In oliguria urinary output is 500 ml per day or less. Oliguria indicates

that the KIDNEYS are not receiving enough blood or are not functioning to filter the blood. Unless urine output increases, toxins will accumulate in the blood and the circumstance may become life-threatening.

See also [ANURIA](#); [UREMIA](#).



percutaneous lithotripsy See [EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY \(ESWL\)](#).

polycystic kidney disease An inherited disorder in which hundreds to thousands of cysts form in the KIDNEYS as well as in other organs and structures such as the LIVER, HEART, and BRAIN. The cysts greatly enlarge and deform the kidneys. The cysts arise from the nephrons, which they destroy as they grow. Polycystic kidney disease affects about 500,000 people in the United States and is the fourth-leading cause of END-STAGE RENAL DISEASE (ESRD). About 10 percent of people on long-term RENAL DIALYSIS have polycystic kidney disease.

The most common type of polycystic kidney disease is autosomal dominant, which affects more than 90 percent of people who have the condition. It occurs as the result of mutations in the PKD1 GENE located on CHROMOSOME 16 and the PKD2 gene on chromosome 4. GENETIC TESTING can detect the presence of these mutations, which confirms the diagnosis. The progression of kidney damage in autosomal dominant polycystic kidney disease typically takes place over decades, with symptoms beginning to manifest around age 30 to 40. A much less common type of polycystic kidney disease is autosomal recessive, which has a different clinical presentation and course of disease. Its symptoms are often present at birth or appear in early childhood.

Symptoms and Diagnostic Path

Autosomal dominant polycystic kidney disease typically shows no symptoms until the person is age 30 to 40. At that time the cysts become numerous enough and large enough to cause PAIN and disrupt kidney function. Urinary system symptoms that emerge include

- HEMATURIA (bloody URINE)
- frequent, recurrent URINARY TRACT INFECTION (UTI)
- kidney stones (NEPHROLITHIASIS)
- upper ABDOMINAL PAIN

Additional symptoms include HYPERTENSION (high BLOOD PRESSURE) resulting from damage to the kidneys and cysts in the liver and other organs. Diverticulosis, a gastrointestinal condition in which small pockets distend from the bowel, is also common. Some people may have deformed heart valves and deformities in blood vessels that cause aneurysms to develop.

Treatment Options and Outlook

Treatment focuses on relieving symptoms. ANTIBIOTIC MEDICATIONS are necessary to treat a UTI. Surgery may be necessary to repair any ANEURYSM and sometimes to reduce the size of the kidneys. Most people progress to ESRD within 10 years of the appearance of symptoms, at which time renal dialysis becomes necessary to sustain life. KIDNEY TRANSPLANTATION is often a viable treatment option. The transplanted kidney does not develop cysts. However, cysts do continue to develop in other organs.

Risk Factors and Preventive Measures

Polycystic kidney disease is both genetic and inherited. People who have this condition in their families may benefit from genetic testing to determine whether they carry the mutated genes, and to discuss their family planning options with a genetic counselor.

See also INHERITANCE PATTERNS; [RENAL CYST](#).

proteinuria See [ALBUMINURIA](#).

pyelonephritis See [NEPHRITIS](#).



renal cancer The growth of a malignant (cancerous) tumor in the kidney. Doctors diagnose about 30,000 people in the United States with renal CANCER, also called kidney cancer, each year. Men are twice as likely as women to get renal cancer, and cigarette smokers (male or female) are two to four times as likely as nonsmokers to get renal cancer. The most common form of renal cancer is renal cell CARCINOMA (RCC), which accounts for more than 90 percent of RCC among Americans. RCC arises from the epithelial cells that line the tubules within the nephrons. A type of kidney tumor that occurs almost exclusively in children under age eight is WILMS'S TUMOR, also called nephroblastoma. Though Wilms's tumor also arises from the tubules, its cells, course of

growth, and treatment options are unique. Cancer from other sites may metastasize to the kidneys.

Symptoms and Diagnostic Path

The earliest indication of renal cancer is HEMATURIA (BLOOD in the URINE), which may be gross (enough blood is present to discolor the urine) or microscopic (the laboratory detects erythrocytes in the urine during examination of the urine sample under the microscope). Other symptoms may include

- lump or swelling in the central abdomen
- fatigue
- abdominal or back PAIN not related to injury
- unexplained or unintended weight loss

STAGING OF RENAL CANCER

Renal Cancer Stage	Extent of Cancer Treatment	Protocols/Options
stage 1	tumor remains confined to one site in one kidney and is 7 cm or smaller	partial or simple NEPHRECTOMY
stage 2	tumor extends beyond the tissue capsule surrounding the kidney or is larger than 7 cm	radical nephrectomy
stage 3	tumor extends to adjacent lymph nodes or the veins that carry BLOOD from the kidney	radical nephrectomy biological therapy
stage 4	tumor extends to both kidneys or to other organs in the abdomen or to distant organs such as the LUNGS OR BRAIN	palliative surgery palliative therapies
recurrent	tumor returns after treatment, appearing either in the same kidney (when first cancer was stage 1), the other kidney, or another location in the body	varies according to previous treatment

- edema (swelling due to retained fluid in the tissues), notably in the hands and feet

The diagnostic path begins with urine tests, blood tests, and abdominal **ULTRASOUND** or **COMPUTED TOMOGRAPHY (CT) SCAN**. Biopsy of the detected tumor confirms the diagnosis and provides information about whether the cancer has yet metastasized. The pathologist assigns the cancer a stage based on the appearance and behavior of its cells. The cancer's stage determines the appropriate treatment options and expected outcome of treatment.

Treatment Options and Outlook

Treatment depends on multiple factors including the person's age, overall health status, and location and stage of the cancer. Doctors generally prefer surgery (**NEPHRECTOMY**) to remove the tumor (stage 0) or the kidney (all other stages). The nephrectomy may be segmental (removal of only the tumor and a small margin of healthy tissue), simple (removal only of the kidney), or radical (removal of the kidney, surrounding tissue, and adjacent **LYMPH NODES**). **CHEMOTHERAPY** and **RADIATION THERAPY** are not very effective in treating renal cancer. Biological therapies such as **INTERFERONS** and **INTERLEUKINS**, which stimulate the **IMMUNE SYSTEM** to step up its attack against the cancer cells, are showing great promise in renal cancer. The oncologist may use biological therapy after surgery for renal cancers that are stage 3 and 4. Some studies suggest a combination of biological therapy and chemotherapy may be more effective than biological therapy alone in some people. Treatment for recurrent renal cancer depends on how and where the cancer returns as well as on previous treatment.

Risk Factors and Preventive Measures

Cigarette smoking is the most identifiable, as well as preventable, risk for renal cancer. Other lifestyle factors that raise an individual's risk for renal cancer include lack of physical exercise (sedentary lifestyle) and **OBESITY**. Researchers believe obesity alters hormonal activity in the body in ways that facilitate the growth of renal cell carcinoma. Other known risks for renal cancer include **POLYCYSTIC KIDNEY DISEASE**, exposure to

asbestos, exposure to heavy metals such as arsenic and cadmium, and industrial chemicals such as benzene and trichloroethylene. Renal cancer is also more common in people between the ages of 50 and 70, and in people who have a family history of renal cancer. The latter suggests genetic involvement, though researchers have yet to confirm evidence of this.

See also **ASBESTOSIS**; **BLADDER CANCER**; **KIDNEYS**; **NEPHRON**; **NEUROTOXINS**; **PROSTATE CANCER**.

renal cyst An encapsulated, fluid-filled growth that occurs in the kidney. Simple renal cysts are common and nearly always benign (noncancerous). Complex renal cysts, which may contain calculi (stones) and **BLOOD**, may be benign or cancerous. Most renal cysts, simple or complex, do not cause symptoms. Rather, the doctor detects them during diagnostic procedures, such as abdominal **ULTRASOUND** or **COMPUTED TOMOGRAPHY (CT) SCAN**, to evaluate other health concerns. When symptoms do occur, they may include a sensation of pressure if the cyst is large enough to pressure other structures in the abdomen or interfere with kidney function. Occasionally, a renal cyst grows large enough or in a location to cause significant **PAIN**.

Ultrasound or CT scan generally provides enough information for the nephrologist to determine whether a renal cyst appears suspicious. A needle biopsy, which removes a small sample of tissue and fluid from the cyst, can show whether the cyst is cancerous. The nephrologist may recommend a course of watchful waiting for benign cysts that cause no symptoms. Surgery is necessary to remove symptomatic or cancerous cysts. Recovery from such surgery—which may be laparoscopic or open, depending on the size and location of the cyst—is generally complete and without complications. The presence of multiple cysts may indicate **POLYCYSTIC KIDNEY DISEASE**, a genetic disorder in which numerous cysts form in the **KIDNEYS** as well as in other organs. Recurrent cysts require further evaluation.

See also **NEPHROLITHIASIS**; **RENAL CANCER**.

renal dialysis Procedures to filter toxins from the **BLOOD** when the **KIDNEYS** are unable to perform this function. Renal dialysis can be short term or

long term. Though in theory renal dialysis could sustain life indefinitely, in practice most people experience a steady decline of overall health with long-term dialysis because artificial methods of cleansing toxins from the blood are not as effective, efficient, or thorough as the natural processes the kidneys perform. However, it is not uncommon for people to use renal dialysis for 10 to 20 years or longer. There are two general types of renal dialysis: hemodialysis and peritoneal dialysis.

Hemodialysis

Hemodialysis filters toxins directly from the blood. The person goes to a hemodialysis center for each dialysis treatment. A catheter inserted into a blood vessel, usually in the arm, routes the blood circulation externally through a machine that removes toxins. The cleansed blood then returns to the body through a second catheter. When hemodialysis is long term, the doctor places a permanent arteriovenous (AV) shunt that connects an ARTERY and a VEIN. The dialysis machine's cannulas then connect to the shunt.

The hemodialysis machine consists of a pump and a container, called the dialyzer with a semiporous membrane inside. The membrane looks somewhat like the filter inside a water purification canister. On one side of the membrane is a solution called the dialysate. The dialyzer pumps blood into the container on the other side of the membrane. The dialysate attracts certain substances—minerals, electrolytes, and waste byproducts—to cross the membrane from the blood. The dialysate absorbs these substances. Fresh dialysate circulates through the dialyzer at the same rate as the blood. The blood and the dialysate never come into direct contact with one another. Another type of filter traps any air bubbles that are in the blood before the blood returns to the body. The dialyzer holds only a few ounces of blood at a time. It takes three to five hours for the blood to circulate through the dialyzer enough times to remove an appropriate amount of waste and toxins. Most people need three hemodialysis sessions every week.

In the United States hemodialysis is the standard renal dialysis method. Many nephrologists feel it more thoroughly cleanses the blood. However, hemodialysis entails significant risks. Key among these risks are INFECTION with HEPATITIS and

other bloodborne conditions, injury to the blood vessels used to shuttle blood between the person and the dialysis machine, and microscopic damage to the blood cells.

Peritoneal Dialysis

Peritoneal dialysis makes use of a natural membrane in the body, the peritoneum, which encloses the abdominal cavity. Peritoneal dialysis is a continuous process. Two catheters surgically inserted into the abdominal cavity serve as the portals through which dialysate enters and leaves the cavity. The doctor prescribes the dialysate, which comes premixed in single-DOSE bags.

The molecules of the dialysate are too large to pass through the peritoneum so the solution remains contained in the abdominal cavity. The blood's natural circulation carries blood through the blood vessels (capillary networks) within the peritoneum. As with hemodialysis, the dialysate attracts certain molecules to cross the membrane into the dialysate. A second catheter carries dialysate out of the abdominal cavity. There are two stages to peritoneal dialysis, the exchange (draining the dialysate into and out of the abdominal cavity) and the dwell (the time during which the dialysate remains in the abdominal cavity).

There are two types of peritoneal dialysis:

- Continuous ambulatory peritoneal dialysis (CAPD) instills dialysate into the abdominal cavity using gravity to pull the dialysate into the catheter. The dialysate remains in the abdominal cavity for about four hours, then the person drains it out through the second catheter. Most people who use this method need four treatments each day. Aside from the 30 minutes it takes to instill the dialysate and the 30 minutes it takes to drain the dialysate, the person is unencumbered and goes about his or her regular activities.
- Continuous cycler-assisted peritoneal dialysis (CCPD) uses a pump to rapidly infuse and extract the dialysate at night when the person is sleeping, with dwell times of about two hours. The person then infuses the abdominal cavity with dialysate upon awakening, and retains the solution all day for a single long dwell time.

The primary advantage of peritoneal dialysis is mobility. Most people are able to participate in regular activities, including work, while peritoneal dialysis is under way, provided the person can perform exchanges on the necessary time schedule and there is a hygienic, private location where the person can do the exchange. The success of peritoneal dialysis is more variable than that of hemodialysis because the permeability of the peritoneum varies among individuals. Some doctors believe peritoneal dialysis is less effective than hemodialysis at clearing toxins from the body.

Benefits and Risks of Renal Dialysis

Renal dialysis is the difference between life and death for people who have END-STAGE RENAL DISEASE (ESRD). For most people, the benefits clearly outweigh the potential risks and complications. The primary risks related to renal dialysis are infection, and, with hemodialysis, bleeding. Renal dialysis becomes less effective over time because it simply is not as effective as the body's natural mechanisms. A slow cascade of complications arises. Dialysis only cleanses the blood; it cannot restore kidney function or prevent further degeneration of the kidneys.

See also QUALITY OF LIFE.

renal failure The inability of the KIDNEYS to adequately filter toxins from the body. Generally the kidneys reach the point of renal failure when they have less than 15 percent functional capacity. Renal failure can be acute (occur suddenly) or chronic (develop slowly over time). Though the term *failure* implies the condition is permanent, but this is not necessarily the case. Most people who experience acute renal failure fully recover with appropriate treatment. When the deterioration of kidney function is progressive and irreversible, however, renal failure is not only permanent but also eventually becomes complete. This irreversible condition is END-STAGE RENAL DISEASE (ESRD). A person who has ESRD requires long-term RENAL DIALYSIS or KIDNEY TRANSPLANTATION to sustain life.

Acute renal failure Acute renal failure can occur in response to any circumstance that overwhelms the body, such as systemic INFECTION,

severe BURNS, or a toxic assault such as a DRUG overdose or massive exposure to a nephrotoxin. DEHYDRATION and lack of BLOOD flow to the kidney (such as may occur with severe ATHEROSCLEROSIS or a blood clot) also can cause acute renal failure. Acute renal failure may require short-term renal dialysis to cleanse the blood while the kidneys recover as well as appropriate treatment for the cause of the renal failure.

COMMON CAUSES OF ACUTE RENAL FAILURE

acute NEPHRITIS	ALCOHOL poisoning
DEHYDRATION	DRUG OVERDOSE
extensive BURNS	gentamicin
HEART FAILURE	HEAT STROKE
HEMOLYTIC UREMIC SYNDROME	LIVER FAILURE
major surgery	multisystem failure
nephrotoxin exposure	reaction to contrast dye
renal ischemia	SEPTICEMIA
streptomycin	trauma

Chronic renal failure Chronic renal failure develops gradually over time, often years to decades. The most common causes of chronic renal failure are NEPHROPATHY of DIABETES and nephropathy of HYPERTENSION (high BLOOD PRESSURE). Other causes include long-term exposure to NEPHROTOXINS, long-term daily use of nephrotoxic drugs such as NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) and other ANALGESIC MEDICATIONS (PAIN relievers), notably codeine. Chronic renal failure may also consist of repeated bouts of acute renal failure that leave minor residual damage. Over time this damage becomes cumulative, causing scarring in the nephrons that impairs their ability to function. About 20 million Americans live with chronic renal failure.

COMMON CAUSES OF CHRONIC RENAL FAILURE

ALPORT'S SYNDROME	chronic HYDRONEPHROSIS
DIABETES	FANCONI'S SYNDROME
GLOMERULONEPHRITIS	GLOMERULOSCLEROSIS
GOODPASTURE'S SYNDROME	HEAVY-METAL POISONING
HYPERTENSION	lupus NEPHROPATHY
organic solvent exposure	POLYCYSTIC KIDNEY DISEASE
renal ARTERY ATHEROSCLEROSIS	RENAL CANCER

Symptoms and Diagnostic Path

Symptoms of renal failure depend on whether renal failure is acute or chronic. Acute renal failure typically causes neurologic symptoms. ANEMIA, hypertension (high blood pressure), congestive HEART FAILURE, and OSTEOPOROSIS (loss of BONE DENSITY and STRENGTH) often accompany chronic renal failure. The diagnostic path includes URINE and blood tests to assess kidney function, diagnostic imaging procedures such as ULTRASOUND and COMPUTED TOMOGRAPHY (CT) SCAN, and often kidney biopsy to microscopically examine the nephrons.

RENAL FAILURE SYMPTOMS

Acute Renal Failure	Chronic Renal Failure
edema	edema
gastrointestinal bleeding	fatigue
confusion	OLIGURIA (diminished URINE production)
loss of consciousness	headaches
seizures	NAUSEA, VOMITING, and loss of APPETITE

Treatment Options and Outlook

Treatment targets the underlying cause. Acute renal failure requires immediate and intensive medical care, often including hemodialysis. Dietary modifications (such as reduced sodium, protein, and fluid intake) and medications to control conditions such as diabetes and hypertension allow many people to live with chronic renal failure for years to decades. When chronic renal failure progresses to ESRD, renal dialysis or kidney transplantation become necessary to sustain life.

Chronic renal failure in children impairs growth because it interferes with the ability of the kidneys to maintain calcium balance within the body and to produce erythrocytes (red blood cells). Without adequate calcium the bones cannot grow, resulting in short stature. Erythrocytes are necessary to carry oxygen, GLUCOSE, and other NUTRIENTS to cells throughout the body. Without these nutrients, cells slow their rate of division. Doctors often prescribe calcitriol supplement, a form of vitamin D, for children who have chronic renal failure to improve the body's ability to retain calcium. Many doctors also prescribe HUMAN

GROWTH HORMONE (HGH) SUPPLEMENT therapy to achieve normal growth patterns in children who have chronic renal failure, though not all doctors agree this is appropriate. Human growth HORMONE supplementation can have other deleterious effects on the body; it is important to balance such risks with the potential benefits.

Risk Factors and Preventive Measures

The major risk factors for chronic renal failure are diabetes and hypertension. Measures to reduce the risk for these conditions also lower the risk for kidney disease. Such measures include

- nutritious EATING HABITS
- daily physical activity
- SMOKING CESSATION
- maintenance of healthy body weight

Diligent control of diabetes or hypertension if these conditions are present can slow their effects on the kidneys. Because chronic renal failure tends to be progressive, it is important to address symptoms of deteriorating kidney function promptly and aggressively for optimal quality of life.

See also HEPATORENAL FAILURE; NEPHROTIC SYNDROME; NEPHRON.

renal tubular acidosis (RTA) A genetic disorder in which the renal tubule within the NEPHRON fails to release hydrogen ions into the filtrate. The consequence is a buildup of acid in the BLOOD (serum acidosis) that causes various symptoms and imbalances among the body's electrolytes. There are numerous forms of renal tubular acidosis (RTA), most of which are random (sporadic) though some types are familial. Common forms of RTA include

- type 1 RTA, which affects the distal tubule and may occur secondary to AUTOIMMUNE DISORDERS such as SJÖGREN'S SYNDROME or after KIDNEY TRANSPLANTATION
- type 2 RTA, which affects the proximal tubule and often accompanies conditions such as WILSON'S DISEASE, FANCONI'S SYNDROME, MULTIPLE MYELOMA, and HYPERPARATHYROIDISM as well as after kidney transplantation

- type 4 RTA, which may accompany NEPHROPATHY of DIABETES or HIV/AIDS, SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), and SICKLE CELL DISEASE

The diagnostic path includes blood tests and URINE tests that measure acidity. Treatment is usu-

ally medication (pharmaceutical sodium bicarbonate) to maintain the blood's pH (acidity level) within the desired range and regular blood or urine tests to measure acidity.

See also GENETIC DISORDERS; [GLOMERULUS](#); [HYPERKALEMIA](#); INHERITANCE PATTERNS.



uremia A serious condition in which nitrogen-based toxins such as urea and creatinine, the primary waste products of METABOLISM, accumulate in the BLOOD because the KIDNEYS are unable to filter them out and pass them from the body via the URINE. Uremia indicates RENAL FAILURE. Urologists sometimes use the term azotemia to designate preclinical uremia—that is, rising levels of urea in the blood that have not yet reached a level at which they cause symptoms.

Symptoms of uremia include

- NAUSEA and VOMITING
- confusion
- HEADACHE
- loss of APPETITE
- lethargy and difficulty concentrating

Blood and urine tests to measure levels of blood urea nitrogen (BUN) and creatinine confirm the diagnosis. Treatment is generally RENAL DIALYSIS to filter metabolic wastes and toxins from the blood, to restore the body's electrolyte, chemical, and water balances. KIDNEY TRANSPLANTATION may be a viable treatment option when kidney failure becomes permanent, such as in END-STAGE RENAL DISEASE (ESRD).

See also [NEPHROPATHY](#); [NEPHROTOXINS](#).

ureter A tubular structure that carries URINE from the kidney to the BLADDER. Urine from the kidney's collecting tubules drains into the renal pelvis, which channels the urine into the ureter. The ureter exits the kidney at the hilus and parallels the inferior VENA CAVA (left ureter) or the AORTA (right ureter) through the abdomen to the pelvis. At the pelvis the ureter crosses over the respective iliac

branches (ARTERY and VEIN) and enters the top back of the bladder. The ureter forms a short, flattened tunnel within the bladder wall before opening into the interior of the bladder. This tunnel functions as a valve to help keep urine from flowing back up the ureter from the bladder. Each ureter is about 12 inches long, though the left is slightly longer than the right as the left kidney sits about an inch higher in the abdomen. The structure of the ureters is the same in men and women.

A smooth epithelial membrane forms the inner lining of the ureter. Two layers of MUSCLE surround the ureteral epithelium, the first running more or less lengthwise (longitudinal) though spiraling widely around the epithelium, and the second wrapping around the ureter in a circular pattern. The outer layer of the ureter is fibrous tissue. The muscle layers of the ureter contract in rhythmic waves (PERISTALSIS) to move urine from the kidneys to the bladder. The ureter is fairly thick and rigid, with an inner diameter of only 3 or 4 millimeters.

For further discussion of the ureters within the context of the urinary system's structure and function please see the overview section "The Urinary System."

See also [GLOMERULUS](#); [KIDNEYS](#); [NEPHRON](#); [URETHRA](#); [VESICoureTERAL REFLUX](#).

urethra A narrow, somewhat muscular tube that carries URINE from the BLADDER to the outside of the body. The point of exit is the urinary or urethral meatus. The urethral sphincter MUSCLE at the base of the bladder controls the release of urine into the urethra. Once the urethral sphincter relaxes to let urine pass, the urine flows to the outside of the body until the bladder empties and the urethral sphincter tightens. It may take a few seconds after the sphincter closes for the residual urine in the

urethra to make its way out the urethral opening. **BLADDER CATHETERIZATION**, **CYSTOSCOPY**, **ureteroscopy**, and **intravesical therapies** use the urethra to enter the urinary system (usually with sedation or **ANESTHESIA**, except catheterization).

In a woman the urethra is about an inch and a half long, extending from the base of the bladder to the external **GENITALIA** where it exits the body between the **CLITORIS** and the **VAGINA**. The urethra's only role in a woman is to carry urine from the body. In a man the urethra is about eight inches long and extends from the base of the bladder to exit the body at the tip of the **PENIS**. As it exits the bladder in a man the urethra passes through the **PROSTATE GLAND**, which encircles the neck of the bladder. The male urethra also carries **SPERM** during **EJACULATION**. The **VAS DEFERENS**, the tube that carries **SEMEN** from the male reproductive organs, enters the urethra at the prostate gland. A valve at the base of the urethra directs the flow of either urine or semen through the urethra.

For further discussion of the urethra within the context of the urinary system's structure and function please see the overview section "The Urinary System."

See also **EPISPADIAS**; **HYPOSPADIAS**; **RETROGRADE EJACULATION**.

urethral stricture Narrowing of the **URETHRA**, impeding the passage of **URINE** from the **BLADDER** to the outside of the body. Urethral stricture may be congenital (present at birth) or acquired such as through scarring resulting from repeated **URETHRITIS**, **BLADDER CATHETERIZATION**, and other irritations to the urethra. **BENIGN PROSTATIC HYPERPLASIA (BPH)** and **PROSTATITIS** also can cause urethral stricture in men.

Symptoms of urethral stricture include

- straining when urinating
- the sensation that the bladder does not empty with **URINATION (URINARY RETENTION)**
- diminished urine flow
- frequent **URINARY TRACT INFECTION (UTI)**

The diagnostic path begins with urinalysis to determine whether **INFECTION** is present. Further

diagnostic procedures may include **CYSTOSCOPY** to examine the urethra and bladder, **INTRAVENOUS PYELOGRAM (IVP)** to assess the flow of **BLOOD** and urine through the urinary system, or **COMPUTED TOMOGRAPHY (CT) SCAN** or **ULTRASOUND** to visualize the structures of the lower pelvis. Treatment targets the identified cause and may include **ANTIBIOTIC MEDICATIONS** when infection is present in addition to other therapies. Such therapies often include cystoscopic surgery to cut away **SCAR** tissue within the urethra or open surgery (**urethroplasty**) to reconstruct a badly scarred or damaged urethra. These methods permanently restore the flow of urine through the urethra and have minimal complications or risks.

See also **UROLITHIASIS**.

urethritis **INFLAMMATION** of an **URETER**. **INFECTION**, typically a sexually transmitted disease (**STD**), is the most common cause of urethritis though urethritis may occur as a result of inflammation or irritation from trauma such as occurs with **BLADDER CATHETERIZATION** or **CYSTOSCOPY**. Traumatic urethritis improves rapidly when the source of the trauma is gone, often without further treatment. Urologists classify infectious urethritis as gonococcal urethritis (**GU**) or nongonococcal urethritis (**NGU**). Symptoms may be vague and transient (disappear in a few days) or nonexistent, though the infection remains. In about 40 percent of women, urethritis progresses to **PELVIC INFLAMMATORY DISEASE (PID)** and **INFERTILITY**. Repeated or untreated urethritis in men may destroy testicular tissue, resulting in sterility. As well, untreated urethritis in men or women remains contagious through sexual contact.

Symptoms and Diagnostic Path

Often urethritis does not have symptoms, particularly in women. When symptoms are present they typically include

- puslike or bloody discharge from the **PENIS**
- **PAIN** or burning with **URINATION (DYSURIA)**

Laboratory analysis of discharge or swabs of the interior of the urethra identify the responsible **PATHOGEN**. Generally no further diagnostic proce-

dures are necessary unless other health concerns coexist.

Treatment Options and Outlook

Treatment is the appropriate antibiotic medication to kill the pathogen. It is important to take the full amount of the antibiotic as prescribed. Though tempting to stop the medication when symptoms abate, incomplete treatment allows the BACTERIA to surge back to reinfect. It also can permit bacteria to develop resistance to commonly prescribed antibiotics, requiring more powerful antibiotics for subsequent treatment. Both GU and NGU can occur repeatedly when the person becomes reinfected. Each cycle of infection requires treatment. It is important (and in many states a legal requirement) to notify sexual partners so they also can receive treatment.

Risk Factors and Preventive Measures

The primary risk for GU and NGU infection is unprotected sex, particularly with multiple partners. Men who have sex with men are at highest risk. Safer sex methods, including the use of a new condom for each sex act, help reduce exposure to the bacteria that cause urethritis though are not foolproof. Traumatic urethritis sometimes becomes chronic in people who must use long-term bladder catheterization, such as those who have SPINAL CORD INJURY resulting in paraplegia. The urologist may prescribe prophylactic antibiotics and anti-inflammatory medications in such situations. Diligent PERSONAL HYGIENE further helps reduce irritation and infection.

See also CHLAMYDIA; CYSTITIS; EPIDIDYMITIS; GONORRHEA; PROSTATITIS; REITER'S SYNDROME; SEXUAL HEALTH; SEXUALLY TRANSMITTED DISEASES (STDs).

urinary diversion A surgical procedure to create a method for the storage and passage of URINE from the body after cystectomy (surgical removal of the BLADDER). Though most often necessary following cystectomy to treat BLADDER CANCER or invasive cancer of the pelvic region, urinary diversion may be necessary after traumatic injury to the bladder. Urinary diversion may also be a palliative treatment for inoperable bladder or pelvic cancer, diverting the flow of urine to overcome

urinary obstruction. Urinary diversion may be continent (collects and contains urine within the body), which most people prefer when it is possible, or incontinent (collects a steady flow of urine in a bag outside the body).

Continent Urinary Diversion

When the urethra remains intact the urologic surgeon can fashion a substitute bladder, called a neobladder, from a segment of bowel (which has the ability to expand somewhat), attaching the ureters and the URETHRA. The neobladder allows the person to urinate naturally. However, the neobladder requires more frequent, and usually timed or scheduled, emptying as it lacks the distention ability and capacity of the native bladder as well as the nerves that activate the micturition REFLEX.

When the cystectomy also includes removal of the urethra, the surgeon generally chooses to craft a collection reservoir from a segment of SMALL INTESTINE that remains in the abdominal cavity, then create a valved opening through the abdominal wall into the reservoir. The person periodically inserts a catheter into the opening to drain the urine, usually every three to four hours, including through the night. Though not as natural as the neobladder, the catheter reservoir still permits urinary continence.

Incontinent Urinary Diversion

Incontinent urinary diversion is similar to the catheter reservoir, except the opening through the abdominal wall, called a stoma, lacks a valve. The person attaches an ostomy bag over the opening using special adhesive. Urine drains continuously into the bag, and periodically the person removes the full bag and replaces it with a clean, empty bag. The bags are small and unobtrusive beneath the clothing. The adhesive ensures there is no leakage of urine. A urostomy bag may require changing every six to eight hours. Surgeons use this method, called urostomy or ileal conduit, primarily when continent urinary diversion is not a viable option.

Outlook and Lifestyle Modifications

Urinary diversion requires diligent attention to hygiene and emptying collected urine. Though the neobladder is the most natural urinary diversion

method, it requires more frequent emptying than would the natural bladder. Likewise the catheter reservoir, which further requires the person to carry a catheter at all times. URINARY TRACT INFECTION (UTI) tend to be more frequent in people who have any form of urinary diversion, though are most common with urostomy. Urostomy also may cause irritation to the SKIN around the stoma. Many people who have urostomies or catheter reservoirs feel self-conscious about them. The urologist or hospital can provide information about support groups where people who have urinary diversions can share their concerns and experiences.

See also [COLOSTOMY](#); ILEOANAL RESERVOIR; ILEOSTOMY; QUALITY OF LIFE; SURGERY BENEFIT AND RISK ASSESSMENT.

urinary frequency The need to urinate more often than normal. Urinary frequency is common in PREGNANCY, CYSTITIS, URINARY TRACT INFECTION (UTI), BENIGN PROSTATIC HYPERPLASIA (BPH) and PROSTATITIS in men, and DIABETES. Urinary frequency at night is NOCTURIA. Sometimes the cause is excessive fluid consumption, particularly in the evening when nocturia is a problem. The diagnostic path may include urinalysis, assessment of any symptoms that accompany the urinary frequency, and procedures such as abdominal ULTRASOUND or CYSTOSCOPY to evaluate the BLADDER and URETHRA. Treatment targets the underlying cause. The doctor may prescribe medications such as tolterodine or oxybutynin to slow the bladder's response when no clear-cut cause emerges and symptoms persist.

See also URINARY INCONTINENCE; URINARY URGENCY.

urinary incontinence The involuntary leakage of URINE from the URETHRA. Health experts estimate that as many as 12 million Americans experience some degree of urinary incontinence, which becomes increasingly common with advancing age. There are several types of urinary continence. They include

- stress incontinence, in which urine leaks with activities such as sneezing, coughing, or laughing
- urge incontinence, in which urine leakage accompanies a sudden and overwhelming desire to urinate

- overflow incontinence, in which the bladder fails to send or respond to the normal NERVE signals that direct urination and becomes overly full, eventually leaking urine because it can hold no more volume

Many people, particularly women past MENOPAUSE, experience a combination of stress and urge incontinence. This combination form of urinary incontinence develops when the pelvic muscles and ligaments that support the bladder weaken and stretch. Overflow incontinence is more common in older men who have BENIGN PROSTATIC HYPERPLASIA (BPH). The enlarged PROSTATE GLAND can constrict the urethra, preventing urine from leaving the bladder. Overflow incontinence may also develop in people who have NEUROPATHY of DIABETES, long-standing chronic ALCOHOLISM, or conditions of the NERVOUS SYSTEM that affect control of involuntary functions such as MULTIPLE SCLEROSIS.

The diagnostic path includes a careful history of the urinary incontinence, BLOOD and urine tests, and possibly diagnostic imaging procedures such as ULTRASOUND or CYSTOSCOPY to identify any underlying conditions that could be causing the urinary incontinence. Treatment may be lifestyle modification, such as altering fluid consumption habits or emptying the bladder on a schedule. Many people, especially women, regain continence with KEGEL EXERCISES to strengthen and tone the pubococcygeal MUSCLE that forms the pelvic floor. Incontinence pads and other items help protect clothing from leaking urine. Sometimes medications to slow the bladder's response, such as oxybutynin (Ditropan), help ease urge incontinence. In situations that do not improve the urologist may suggest surgery to tighten pelvic muscles or the urethral sphincter. Though finding the most effective solution may take time, most people are able to successfully manage urinary incontinence.

See also [ENURESIS](#).

urinary retention The inability to completely empty URINE from the BLADDER with URINATION. Because urinary retention presents a risk for bacterial URINARY TRACT INFECTION (UTI) or NEPHRITIS (INFECTION of the KIDNEYS), it is important to find and treat its cause. The most common cause is an

obstruction that blocks or narrows the URETHRA such as a bladder stone (UROLITHIASIS), URETHRITIS or URETHRAL STRICTURE, BENIGN PROSTATIC HYPERPLASIA (BPH) or PROSTATITIS in men, CYSTOCELE (sagging of the bladder) or UTERINE PROLAPSE in women, and rarely a tumor. As well, STROKE, SPINAL CORD INJURY, or TRAUMATIC BRAIN INJURY (TBI) can damage the nerves that control urination. The diagnostic path may include urinalysis and CYSTOSCOPY or ULTRASOUND to evaluate the urethra and bladder. Treatment targets the underlying cause and may include BLADDER CATHETERIZATION to empty the bladder of urine, either as an emergency procedure for acute urinary retention or on a routine basis for chronic urinary retention. Often, the underlying cause is treatable and the urinary retention resolves.

See also [URINARY FREQUENCY](#); URINARY URGENCY.

urinary urgency The overwhelming sensation of the need to urinate. Urinary urgency, also called overactive BLADDER, can cause a person to urinate dozens of times each day. Though a common symptom of conditions such as CYSTITIS and URINARY TRACT INFECTION (UTI), especially when urinary urgency occurs in combination with URINARY FREQUENCY, urinary urgency may indicate a blockage in the urinary tract or result from neurologic conditions or injuries. Urinary urgency may also result in URINARY INCONTINENCE (inability to hold the URINE), even when the amount of urine in the bladder is small. Other common causes include DIABETES, PREGNANCY in women and BENIGN PROSTATIC HYPERPLASIA (BPH) in men. The diagnostic path begins with an assessment of any symptoms that accompany the urinary urgency, urinalysis, and perhaps procedures such as CYSTOSCOPY and pelvic ULTRASOUND to examine the bladder and URETHRA. Treatment targets any identified underlying cause. The doctor may prescribe medications such as tolterodine or oxybutynin to slow the bladder's response.

See also [NEUROGENIC BLADDER](#); URINARY RETENTION.

urinary tract infection (UTI) A bacterial INFECTION of the BLADDER and URETHRA. The most common bacterial culprit is *Escherichia coli*, which is normally present in the gastrointestinal tract. Other BACTERIA may also cause UTI. Typically UTI,

commonly called bladder infection, refers to infection that remains in the bladder and urethra. UTI may be acute (come on suddenly) or chronic (occur repeatedly over time). Untreated or under-treated UTI can spread into the KIDNEYS (NEPHRITIS), causing significant illness and the potential for permanent damage to the delicate tubules and glomeruli of the nephrons.

Symptoms and Diagnostic Path

Symptoms of acute UTI tend to be more intense than symptoms of chronic UTI, though either can be highly uncomfortable. The general symptoms of UTI include

- DYSURIA (burning with URINATION)
- URINARY FREQUENCY and URINARY URGENCY
- HEMATURIA (bloody URINE)
- cloudy, foul-smelling urine
- aching or discomfort in the lower pelvis or lower back

Urinalysis shows the presence of bacteria in most UTIs, confirming the diagnosis. Urinalysis does not identify the kind of bacteria, however. The doctor may choose to obtain a urine sample via BLADDER CATHETERIZATION (to avoid contamination by bacteria normally on the SKIN's surface) and culture it in the laboratory to determine the kind of bacteria present. A urine culture is especially helpful in chronic UTI or when symptoms fail to respond to initial treatment. A urologist may recommend additional diagnostic procedures for chronic UTI to determine the underlying reasons for the frequency or persistence of infection.

Treatment Options and Outlook

ANTIBIOTIC MEDICATIONS are the standard treatment for UTI. The antibiotic and length of treatment depend on the bacteria causing the infection. Most UTIs in women respond to a 3-day course of the antibiotic TMP-SMX or an antibiotic in the fluoroquinolone family such as ciprofloxacin. Women who cannot take either of these antibiotics may instead take an antibiotic in the tetracycline family (tetracycline or doxycycline) or the cephalosporin family (such as cefaclor). Men take the same antibiotics though often require a longer course,

typically 7 to 10 days. It is important to continue taking all prescribed doses of the antibiotic, even when symptoms improve, to make sure the antibiotic kills all the bacteria. The doctor may prescribe low-DOSE antibiotic medications for long-term preventive therapy (six months to a year) in women who have recurrent UTIs.

The medication phenazopyridine, a topical anesthetic that numbs the inner lining of the bladder and urethra, relieves discomfort during the first 36 to 48 hours of the UTI until the antibiotic begins eliminating bacteria. Phenazopyridine colors the urine deep orange and stains clothing. Some people experience intense bladder spasms, for which the doctor may prescribe a short course of antispasmodic medications such as flavoxate or methenamine.

ANTIBIOTICS COMMONLY PRESCRIBED TO TREAT UTI		
amoxicillin	cefaclor	cefixime
cefotaxime	cefepodoxime	cefprozil
cefuroxime axetil	ciprofloxacin	doxycycline
fosfomycin	levofloxacin	nitrofurantoin
norfloxacin	ofloxacin	sparfloxacin
sulfamethoxazole	tetracycline	TMP-SMX
trimethoprim		

Risk Factors and Preventive Measures

UTIs are common in girls and women though uncommon in boys and men because of differences in anatomy. The very short female urethra provides an easy route for bacteria to travel into the bladder. Health experts estimate that one in five women will have at least one UTI during her lifetime. Measures to reduce the risk for UTI include

- drinking enough water (six to eight 8-ounce glasses daily)
- urinating when the bladder signals it is full
- wiping with toilet tissue from front to back
- urinating soon after SEXUAL INTERCOURSE
- prophylactic antibiotics when UTI occurs three times in a year or more frequently

About 20 percent of women who have one UTI have another; recurrent UTI is rare in men. Though untreated or undertreated UTI can cause

serious and permanent damage to the urinary system, people who have appropriately treated UTIs typically recover completely and without residual complications.

See also CYSTITIS; GLOMERULUS; NEPHRON; SEXUALLY TRANSMITTED DISEASES (STDs); URETHRITIS.

urination The act of passing URINE from the BLADDER, also called uresis or micturition. Urination occurs when the urethral sphincter relaxes at the same time the detrusor MUSCLE that forms the middle layer of the bladder wall contracts, squeezing urine into the URETHRA. The urethra carries the urine to the meatus, its opening on the outer surface of the body. In men the meatus is at the tip of the PENIS; in women the meatus is within the VULVA between the CLITORIS and the VAGINA. Urination ends when the bladder sphincter closes and the residual urine in the urethra passes from the body.

Urination is a blend of involuntary and voluntary control. At birth urination is completely under the control of the micturition REFLEX and the sympathetic NERVOUS SYSTEM, which regulates involuntary functions. The micturition reflex is the series of events that begins when the filling of the bladder with urine activates specialized nerves in the bladder wall called stretch receptors. The stretch receptors send NERVE signals out to the SPINAL NERVES (S2, S3, and S4) that control the urethral sphincter and the detrusor muscle. The spinal nerves send back the nerve signals that stimulate the detrusor muscle to contract and the urethral sphincter to relax. A structure within the pons of the brainstem, the pontine micturition center (PMC), coordinates these functions to occur simultaneously.

The ability to control urination becomes possible around the ages of three to five when the muscles and nerve paths mature. At this point of development the BRAIN can override the involuntary nerve processes and the pubococcygeal muscle, which is a voluntary muscle, can override the involuntary muscle functions of the bladder. The normal frequency of urination varies among individuals and with fluid consumption, which largely determines urine volume. A healthy adult produces between 1.5 and 3 liters of urine every 24 hours. Typically the stretch receptors respond when the bladder contains about 200 to 300 milli-

liters of urine; maximum capacity of the bladder is about 500 ml.

CONDITIONS OF ALTERED URINATION	
ANURIA	DYSURIA
HEMATURIA	NOCTURIA
URINARY FREQUENCY	URINARY INCONTINENCE
URINARY RETENTION	URINARY URGENCY

See also [NEUROGENIC BLADDER](#).

urine The liquid the [KIDNEYS](#) generate to pass wastes and excess fluid from the body. The typical adult makes and passes between 1,500 and 3,000 milliliters (1.5 to 3 liters) of urine every 24 hours. Numerous variables influence the volume and composition of urine, though in general urine is 95 percent water and 5 percent suspended or dissolved solids.

Most of the solids urine contains are organic wastes in the forms of urea, uric acid, creatinine, and ammonia. These are the nitrogen-based waste byproducts of [METABOLISM](#) that the kidneys filter from the [BLOOD](#). The urine also contains minerals (electrolytes) the kidneys excrete to maintain the body's electrolyte and fluid balance. Excreted electrolytes include sodium, potassium, chloride, magnesium, phosphate, and calcium. Normal urine may contain small amounts of [ALBUMIN](#) (protein).

Urine of normal concentration is pale yellow and has no odor. Dilute urine is colorless; concentrated urine can appear dark yellow to orange. Dietary substances, certain medications, and certain health conditions can alter the color as well as the odor of the urine. Normal urine is slightly acidic and has a specific gravity of 1.010 to 1.025, slightly above that of water. Deviations from normal urine composition and concentration suggest various health conditions and may require diagnostic evaluation.

For further discussion of the urine within the context of the urinary system's structure and function please see the overview section "The Urinary System."

See also [ALBUMINURIA](#); [ANURIA](#); [CYSTINURIA](#); [HEMATURIA](#); [OLIGURIA](#); [UREMIA](#); [UROLITHIASIS](#).

urolithiasis The formation of calcifications (also called calculi) in the [BLADDER](#). Most bladder stones,

like kidney stones, form of calcium in combination with oxalate (the most common combination), phosphate, or magnesium. Bladder stones are less common today than kidney stones ([NEPHROLITHIASIS](#)), though throughout recorded history bladder stones have been a common urologic condition. Bladder stones are most likely to form when [URINE](#) remains in the bladder for an extended time, particularly with [URINARY RETENTION](#) (in which the bladder fails to completely empty with [URINATION](#)). [URETHRAL STRICTURE](#), [CYSTOCELE](#), [BENIGN PROSTATIC HYPERPLASIA \(BPH\)](#), long-term [BLADDER CATHETERIZATION](#), and [NEUROGENIC BLADDER](#) are among the conditions that contribute to the formation of bladder stones. Chronic [DEHYDRATION](#), such as occurs with drinking too little water, further contributes to calcification. Bladder stones are also common during [PREGNANCY](#).

In urinary stasis the minerals dissolved in the urine begin to settle out when the urine is static (not moving), forming crystals. The formed crystals attract more of their composite minerals, eventually hardening into calculi. Small stones often easily pass through the urethra in the urine without the person's awareness of them. Stones that are large enough to scrape the walls of the urethra, or sandlike clumps of calculi that surge through the [URETHRA](#), may cause irritation such as [DYSURIA](#) (burning sensation) with urination. Other symptoms may include [URINARY FREQUENCY](#), [URINARY URGENCY](#), and urinary hesitation (difficulty starting urination, or start-and-stop urination).

A stone that completely blocks the urethra, often at the neck of the bladder, causes excruciating [PAIN](#) that may feel as though it arises in the groin or, in men, in the [TESTES](#) (testicles). Often a change in position relieves the pain, causing the urine to wash the stone from its point of occlusion. A stone that is larger than the diameter of the urethra will intermittently though persistently obstruct the passage of urine. It may also cause bleeding, resulting in [HEMATURIA](#) (blood in the urine).

The diagnostic path typically includes urinalysis, [ULTRASOUND](#) to detect the presence of stones in the bladder, and [CYSTOSCOPY](#). Cystoscopy often is both diagnostic and therapeutic, allowing the urologist to confirm the presence of stones as well as remove them from the bladder. Larger stones may require treatments such as [EXTRACORPOREAL SHOCKWAVE](#)

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LITHOTRIPSY (ESWL) or surgical procedures such as percutaneous lithotomy or open cystostomy to remove the stones. Most people recover fully. Bladder stones tend to recur, however.

See also [CYSTINURIA](#); [HYPERCALCIURIA](#); [HYPEROX-ALURIA](#).

urostomy See [URINARY DIVERSION](#).



vesicoureteral reflux A condition in which URINE backflows from the BLADDER into the ureters toward the KIDNEYS. Vesicoureteral reflux may result from congenital anomalies in the structure of the ureters, such as short ureters or ureters that enter the bladder wall in an unusual location or at an unusual angle. Normally the URETER forms a short, flattened tunnel within the bladder wall that functions like a valve to keep urine from reentering the ureter from the bladder. Structural anomalies may prevent the valvelike action of the ureter's entrance into the bladder from functioning properly, such that when the bladder fills

with urine the ureter is open and allows urine to enter.

Vesicoureteral reflux may also develop secondary to an obstruction that blocks the flow of urine from the bladder, such as bladder stones (UROLITHIASIS) or an enlarged PROSTATE GLAND in a man. Such an obstruction causes the bladder to overdistend, which causes the ureteral tunnels to open and allow urine to enter the ureters. INFECTION that inflames and narrows the URETHRA also can obstruct the flow of urine out of the bladder. Vesicoureteral reflux presents a high risk for INFLAMMATION and bacterial infection of the kidneys

VESICoureTERAL REFLUX GRADING		
Reflux Grade	Extent of Urine Reflux	Effect on Kidneys
grade 1	part way up URETER but not into the kidney	increased risk for NEPHRITIS
grade 2	completely up ureter to renal pelvis	increased risk for nephritis
grade 3	URINE backs up into the renal pelvis and renal calyces	mild dilation of renal pelvis and ureters mild nephritis likely
grade 4	urine distends the renal pelvis and renal calyces	significant dilation of ureters nephritis HYDRONEPHROSIS with mild to moderate impaired renal function risk of permanent kidney damage
grade 5	as much or more urine refluxes as passes from the URETHRA	extensive and persistent dilation of ureters, renal pelvis, and renal calyces nephritis hydronephrosis with significant impaired renal function secondary problems such as HYPERTENSION permanent kidney damage likely

(NEPHRITIS) by introducing into the kidneys BACTERIA that may be present in the urine. Vesicoureteral reflux also can cause HYDRONEPHROSIS, dilation of the renal pelvis that results from the accumulation of urine. Nephritis and hydronephrosis both can cause permanent and sometimes progressive kidney damage.

Symptoms and Diagnostic Path

The most common indication of vesicoureteral reflux is infection, the symptoms of which typically include

- flank or ABDOMINAL PAIN
- FEVER and chills
- HEMATURIA (BLOOD in the urine) or cloudy urine
- DYSURIA (discomfort with URINATION)
- urinary frequency and urinary urgency

As well, the person may strain when urinating and feel as though urine remains in the bladder (URINARY RETENTION) after urinating. The diagnostic path begins with urinalysis, which shows the presence of bacteria, leukocytes (white blood cells that fight infection), and erythrocytes (red blood cells) when there is an infection. The urologist may perform diagnostic imaging procedures, such as abdominal ULTRASOUND or COMPUTED TOMOGRAPHY (CT) SCAN, to visualize the structures of the urinary system and identify any anomalies. Radionuclide scan, INTRAVENOUS PYELOGRAM (IVP), and voiding CYSTOURETHROGRAM are additional diagnostic procedures that help the urologist assess the urinary system's structure and function. Diagnosis of vesi-

coureteral reflux includes the designation of grade, which denotes the severity of the urine reflux and the effect on the kidneys.

Treatment Options and Outlook

Infection requires immediate treatment with ANTIBIOTIC MEDICATIONS. When the vesicoureteral reflux occurs secondary to an obstructive condition, treatment targets the underlying cause as well as any consequential infection. Treatment for primary vesicoureteral reflux depends on the person's age and the grade of the reflux. Children are likely to outgrow grade 1 and grade 2 reflux when the cause is short ureters and often when the cause is unusual entry of the ureters into the bladder. Grade 3 reflux may require corrective surgery. Grade 4 and grade 5 refluxes require reconstructive surgery such as ureteroneocystostomy, in which the surgeon creates new insertion tunnels into the bladder for the ureters. Appropriate treatment reduces the risk for permanent damage to the kidneys and restores the normal flow of urine.

Risk Factors and Preventive Measures

In children the primary risk factors for vesicoureteral reflux are anomalies of structure within the urinary system; these are not preventable. In adults risk factors for vesicoureteral reflux include NEPHROLITHIASIS (kidney stones), urolithiasis, chronic URINARY TRACT INFECTION (UTI), and BENIGN PROSTATIC HYPERPLASIA (BPH) in men. Prompt and appropriate treatment for these conditions reduces the risk they will cause vesicoureteral reflux.

See also [BLADDER EXSTROPHY](#); [CONGENITAL ANOMALY](#); [SURGERY BENEFIT AND RISK ASSESSMENT](#).



Wilms's tumor A malignant (cancerous) growth in the kidney. Wilms's tumor, also called nephroblastoma, nearly always affects children under age six. Though relatively rare, with doctors diagnosing about 500 children a year in the United States with this form of kidney cancer, Wilms's tumor is the most common cancer of the kidney that occurs in children. Current treatment approaches have much improved survival, with the five-year survival rate now exceeding 90 percent.

Symptoms and Diagnostic Path

Wilms's tumor may not show symptoms until it is quite large, at which point a parent or caregiver may see or feel the tumor as a lump in the child's belly. The pediatrician may discover Wilms's tumor during a routine well-child examination. When the tumor causes symptoms, they often include

- HEMATURIA (bloody URINE)

STAGING OF WILMS'S TUMOR

Wilms's Tumor Stage	Extent of Cancer	Treatment Protocols/Options
stage 1	tumor is small and remains localized in one kidney	partial or simple NEPHRECTOMY followed by CHEMOTHERAPY
stage 2	tumor extends beyond the kidney though remains confined to a single mass that surgery can completely remove	radical nephrectomy followed by chemotherapy
stage 3	tumor extends to adjacent structures and lymph nodes and surgery cannot completely remove it	chemotherapy before surgery radical nephrectomy followed by chemotherapy and possibly RADIATION THERAPY
stage 4	tumor has metastasized to distant sites	chemotherapy nephrectomy radiation therapy
stage 5	both KIDNEYS have tumors	partial nephrectomy of both kidneys to remove as much cancer as possible yet retain kidney function chemotherapy repeat partial nephrectomy radiation therapy
inoperable	tumor is very large or located too close to vital BLOOD vessels for surgery to be viable	chemotherapy, radiation therapy, or a combination to reduce the tumor's size

- decreased APPETITE and weight loss
- NAUSEA and VOMITING
- abdominal discomfort or PAIN
- generalized irritability and crankiness

The diagnostic path begins with a comprehensive physical examination, BLOOD tests, and urinalysis. Diagnostic imaging procedures such as ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, or MAGNETIC RESONANCE IMAGING (MRI) can identify the presence, size, and location of the tumor. Biopsy of the tumor is necessary to confirm the diagnosis.

Microscopic examination of the biopsied tissue further allows the pathologist to determine whether the tumor's cells are anaplastic, which means they are highly irregular and divide both rapidly and erratically. Tumors of anaplastic cells may be diffuse through the kidney and are more difficult to treat than tumors of what pathologists call favorable cells (cancerous cells that are more pathologically normal). The pathologist also assigns the cancer a grade that identifies the extent to which the tumor has spread (metastasized), which helps determine the appropriate treatment options.

Treatment Options and Outlook

NEPHRECTOMY (surgery to remove the affected kidney) in combination with CHEMOTHERAPY is the standard treatment for Wilms's tumor cancers. Partial nephrectomy removes the tumor and a margin of kidney tissue around it; simple nephrectomy removes the entire kidney. Radical nephrectomy removes the kidney. The oncologist may also add RADIATION THERAPY when the cancer's stage is advanced or its cells are anaplastic regardless of stage.

When the tumor is very large or the cancer involves both KIDNEYS, the oncologist may recommend chemotherapy or radiation therapy (or a combination of both) before surgery to shrink the tumors as much as possible. The oncologist may suggest participation in a clinical trial for inoperable, stage 5, or recurrent Wilms's tumor.

Treatment success largely correlates to the stage of the Wilms's tumor (the size of the tumor and

the extent to which it has metastasized) and the characteristics of the cancer cells (anaplastic or favorable) at the time of diagnosis. Wilms's tumor is among the childhood cancers doctors consider curable.

Risk Factors and Preventive Measures

Researchers have recently identified GENE mutations that account about 30 percent of Wilms's tumor cancers. Located on CHROMOSOME 11, these are the Wilms's tumor 1 (WT1) and 2 (WT2) genes and provide encoding for development of urinary and genital structures. Wilms's tumor also is associated with several rare genetic syndromes, making it likely that other gene mutations further contribute to the errant encoding that allows these primitive cells to thrive. Family history raises the risk for Wilms's tumor, as it appears the gene mutations are sometimes hereditary.

Researchers believe Wilms's tumor represents clusters of cells in the kidneys that remain primitive, a consequence of the WT1 and WT2 mutations. When these primitive cells divide, they continue to do so at the same rapid rate of cell division that was normal in the EMBRYO. In the older child's body, however, this is inappropriate and the cells grow out of control, some wildly (the anaplastic cells). Some researchers believe the cell growth continues from early developmental stages and ultimately manifests as a tumor when the cluster of cells achieves enough mass. Other researchers believe environmental factors, perhaps processes in the body related to growth, trigger the cells to resume dividing.

There are no measures to prevent Wilms's tumor. Families who have had children with Wilms's tumor should have any other children undergo regular routine medical examinations that include screening (such as ultrasound) for the cancer. Doctors do not yet know the long-term health implications for Wilms's tumor survivors as the treatments that make survival possible have not been available long enough for many survivors to have yet reached adulthood.

See also [BLADDER CANCER](#); [CANCER TREATMENT OPTIONS AND DECISIONS](#); [MUTATION](#); [RENAL CANCER](#); [SURGERY BENEFIT AND RISK ASSESSMENT](#).

THE REPRODUCTIVE SYSTEM

The organs and functions of the reproductive system make possible the creation of new life. Physician specialists who treat health conditions of the male reproductive system are urologists. Physician specialists who treat health conditions of the female reproductive system are gynecologists. Health-care providers who provide care during PREGNANCY and CHILDBIRTH are obstetricians (physician specialists) and midwives (usually registered nurses). Nurse practitioners (registered nurses with advanced specialized training and credentials) often function as women's health-care specialists, providing routine wellness care and treatment for minor reproductive and SEXUAL HEALTH conditions.

This section, “The Reproductive System,” presents a discussion of the organs and structures of the male and female reproductive systems, an overview of reproductive and sexual health and disorders, and entries about the health conditions that involve the male and female reproductive systems. “The Urinary System” contains entries about male organs and structures that share urinary and reproductive functions. “Genetics and Molecular Medicine” contains entries about the genetics of reproduction. “The Endocrine System” contains entries about the sex hormones.

Structures of the Female Reproductive System

BREAST	fimbriae
nipple	UTERUS
areola	CERVIX
lactiferous glands	VAGINA
lactiferous ducts	Bartholin's glands
OVARIES	hymen
ovum	labia
FALLOPIAN TUBES	CLITORIS

Structures of the Male Reproductive System

PENIS	TESTICLES
foreskin	SPERM
glans	epididymis
meatus	VAS DEFERENS
URETHRA	PROSTATE GLAND
corpora cavernosa	seminal vesicle
corpus spongiosum	urethra
SCROTUM	

Functions of the Reproductive System

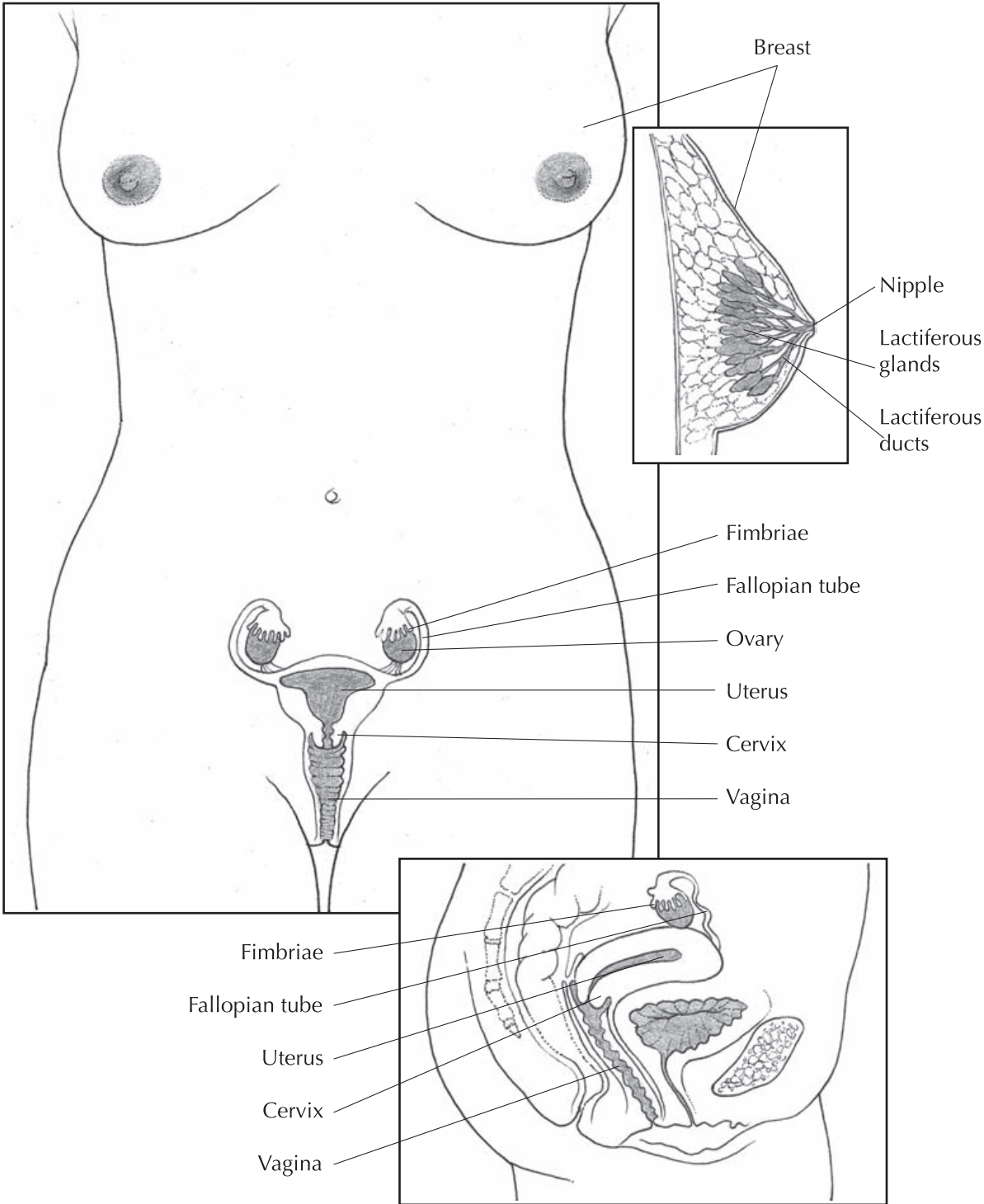
Human reproduction requires participation from both male and female, each of which contributes one half the genetic material necessary for human existence. The cells that carry this material are the gametes—the OVA, or eggs, from the female half and the spermatozoa, or SPERM, from the male half. Determining gender are the sex chromosomes, one from each gamete to form the pair that designates the gender of the new life. Though gender distinction is apparent at birth, functional characteristics of gender do not emerge until late childhood when hormonal shifts initiate the changes of PUBERTY. At puberty the levels of androgens and estrogens increase in the body, initiating the emergence of the secondary sexual characteristics that mark reproductive maturity.

From a common beginning: embryonic gender differentiation The glands that both represent and sustain gender are the gonads—the OVARIES in the woman and TESTICLES, or testes, in the man. In the embryo these structures arise from the same base cells in the mesoderm (the middle layer of germ cells in the embryo) called the gonadal ridge. Until seven weeks, the embryo is androgynous (has no gender characteristics; male and female appear the same) with rudimentary structures—the genital tubercle, labioscrotal swellings, and urogenital groove and folds—that will evolve into gender-appropriate organs as the embryo develops.

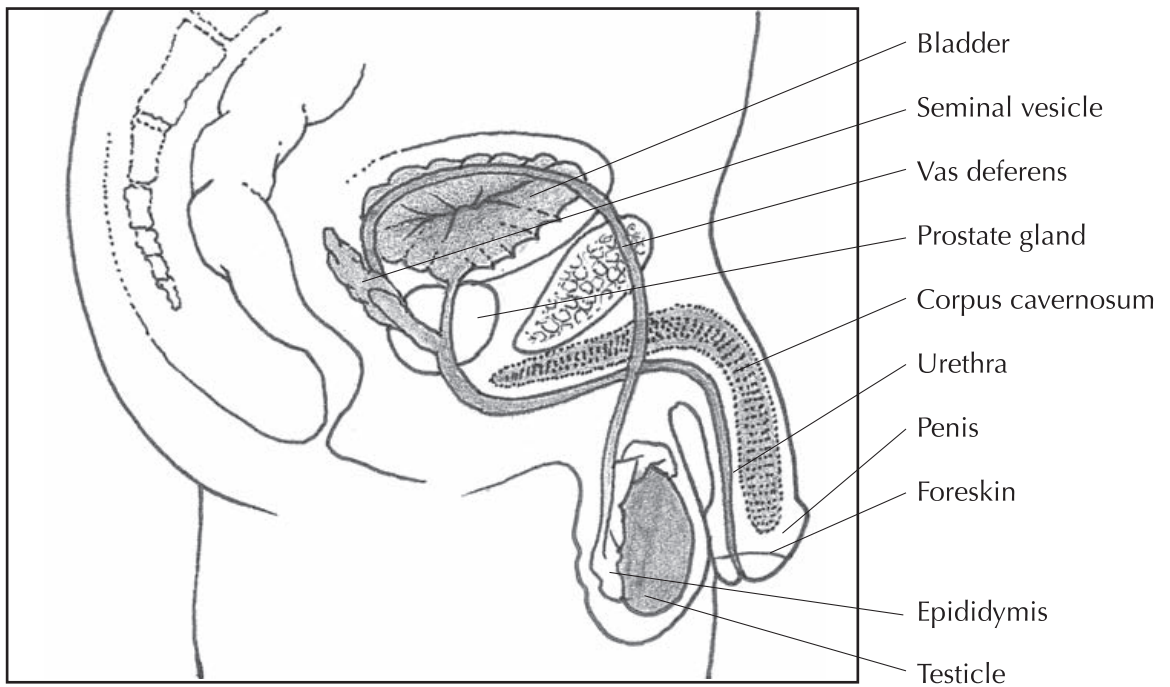
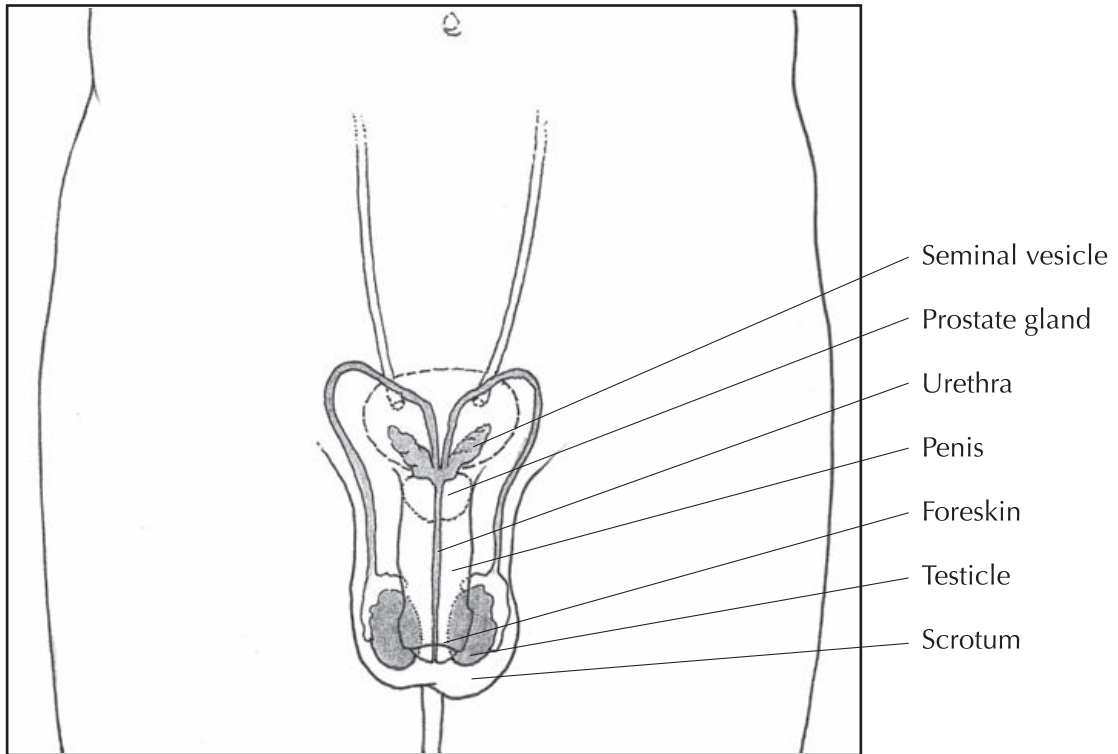
At seven weeks the gonadal ridge organizes into a two-layer structure. If the genetic composi-

The Female Reproductive System

Female



The Male Reproductive System



tion of the embryo is male, the gonadal ridge begins to produce TESTOSTERONE and a hormone unique to embryonic development, müllerian-inhibiting hormone. In response to testosterone the inner layer, the medulla, begins to take shape as the testes and the outer layer, the cortex, degenerates. The genital tubercle becomes the glans PENIS, the urogenital groove and folds enlarge to form the rest of the penis, and the labioscrotal swellings fuse to form the SCROTUM.

If the embryo's genetic composition is female there is no secretion of testosterone and müllerian-inhibiting hormone. So instead the outer layer, the cortex, begins to develop into the ovaries and the medulla deteriorates. The genital tubercle becomes the CLITORIS, the urogenital groove and folds become the VAGINA and labia minora, and the labioscrotal swellings form the labia majora. Primordial germ cells from the yolk sac migrate into the evolving testes or ovaries to become gametes (ova or sperm) as development continues. By 12 weeks gender differentiation is complete, though gender does not become detectable with ULTRASOUND imaging until the 20th week or later.

THE MYTHOLOGY OF THE HYMEN

The hymen, a narrow ring of membranous tissue that extends across the opening of the VAGINA, derives from the Greek god of the wedding feast, Hymen (also Hymenaeus). Hymen was the progeny of Dionysus, the god of FERTILITY, and Aphrodite, the goddess of love. Though the belief persists today that an intact hymen is evidence of a woman's virginity, in truth numerous activities (tampon use, horseback riding, bicycling, and gymnastics to name a few) can rupture the hymen. As well, the structure of the hymen varies widely among women and may be so insignificant as to not impede the penetration of the erect PENIS.

Transition to fertility: puberty Despite genital differences, boys and girls are fairly much alike physiologically for a dozen years or so after birth. Then hormonal signals trigger the onset of puberty, the transition from childhood to sexual and reproductive maturity. Though researchers do not know what activates the hormonal signals, the

consequences are very familiar: the emergence of SECONDARY SEXUAL CHARACTERISTICS. The ovaries and testicles again become active, initiating the anatomic and physiologic changes that transform boys to men and girls to women. With sexual and reproductive maturity complete, SEXUAL INTERCOURSE and pregnancy become possible.

New life: conception, pregnancy, and childbirth

On the surface of it, reproduction is an astonishingly simple premise, and its organs uniquely suited to its purpose. During sexual intercourse the erect penis fits precisely within the vagina, reaching to the CERVIX. EJACULATION deposits millions of sperm in the upper vagina, a short swim from the cervical os (opening through the cervix into the UTERUS). When conditions and timing are right, the sperm make their way through the cervix and uterus and into one of the FALLOPIAN TUBES, encounter the ovum (egg), and one of the millions penetrates the ovum to fertilize it. The resulting ZYGOTE travels down the fallopian tube, tumbles into the uterus, and implants itself into the dense, spongy endometrium: CONCEPTION.

The woman's body nourishes and shelters the developing FETUS, expanding and changing to accommodate its needs. The uterus stretches up to 10 times its normal size, pushing the abdominal wall outward. Again it is hormones that facilitate and support these processes, and hormones that bring the pregnancy to its conclusion: childbirth.

In the process of it, of course, there is nothing simple about any dimension of reproduction. Reproduction represents one of the most intricately choreographed experiences the human body can accommodate. Hundreds of hormones direct countless interactions, each of which spurs other events. Numerous factors, internal and external, influence reproduction to make it possible or not possible. Among the most significant advances in reproductive medicine are technologies to assist the process at various points along the reproductive continuum, from fertilization through childbirth.

Completing the cycle: menopause Men remain fertile nearly the rest of their lives after puberty, though sperm production and quality tend to diminish in later life as testosterone levels decrease. FERTILITY ends for women with MENOPAUSE, the cessation of OVULATION and men-

strual cycles. The ovaries contain a finite number of ova, present at birth. From the onset of MENSTRUATION to midlife, each monthly cycle causes a half dozen to a dozen ovarian follicles to ripen. Usually only one ovum (egg) reaches full maturity and leaves the ovary; the others atrophy (shrink) and the ovary reabsorbs them. By midlife the ovaries have made it pretty much through their supply of ova, far fewer follicles activate with each MENSTRUAL CYCLE, and ovarian function begins to shut down. Over a period of five to eight years, menstrual cycles become irregular and eventually infrequent until they stop altogether.

Health and Disorders of the Reproductive System

The health of the reproductive system, male or female, experiences internal and external influences. Internally the reproductive system relies significantly on an intricate hormonal balance as hormones direct nearly all sexual and reproductive functions. Disorders are often endocrine in origin. The organs of reproduction are particularly vulnerable to cancers that thrive on hormones, such as BREAST CANCER, OVARIAN CANCER, ENDOMETRIAL CANCER, PROSTATE CANCER, and TESTICULAR CANCER. Externally the reproductive system is vulnerable to injury and illness, to great extent through sexual activity. SEXUALLY TRANSMITTED DISEASES (STDs) can cause serious and sometimes life-threatening health conditions. STDs are a leading cause of INFERTILITY in women and can cause illness in newborns who are exposed during birth. Other factors that can affect reproductive health include exposures to chemicals such as pesticides or to radiation, which can damage the DNA of sperm or ova.

External factors are particularly important during pregnancy, when certain exposures at vulnerable points of fetal development can cause permanent injury. INFECTION with common viruses such as RUBELLA (German MEASLES) or measles can cause devastating BIRTH DEFECTS, as can taking certain drugs and medications. Nearly any substance the woman takes into her body may cross the PLACENTA to enter the fetus's BLOOD circulation. FETAL ALCOHOL SYNDROME, a constellation of physical birth defects and developmental abnormalities that occurs as a result of fetal exposure to ALCOHOL, is entirely preventable.

HEALTH CONDITIONS OF THE REPRODUCTIVE SYSTEM

ADENOMYOSIS	AMENORRHEA
BALANITIS	BARTHOLIN CYST
BENIGN PROSTATIC HYPERPLASIA (BPH)	BREAST CANCER
CERVICAL CANCER	CANCER OF THE PENIS
CHORDEE	CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN)
CRYPTORCHIDISM	DYSMENORRHEA
ECLAMPSIA	ECTOPIC PREGNANCY
ENDOMETRIAL CANCER	ENDOMETRIAL HYPERPLASIA
ENDOMETRIOSIS	EPIDIDYMITIS
ERECTILE DYSFUNCTION	fibroadenoma
FIBROCYSTIC BREAST DISEASE	GYNECOMASTIA
HEMATOSPERMIA	HYDROCELE
HYPOGONADISM	INFERTILITY
INTRADUCTAL PAPILLOMA	KLINEFELTER'S SYNDROME
MASTALGIA	MASTITIS
NABOTHIAN CYST	NEONATAL JAUNDICE
ORCHITIS	OVARIAN CANCER
OVARIAN CYST	PAGET'S DISEASE OF THE BREAST
PARAPHIMOSIS	PEYRONIE'S DISEASE
PHIMOSIS	POLYCYSTIC OVARY SYNDROME (PCOS)
PREECLAMPSIA	PREMENSTRUAL SYNDROME (PMS)
PREMATURE OVARIAN FAILURE	PROSTATITIS
PRIAPISM	SEXUALLY TRANSMITTED DISEASES (STDs)
PROSTATE CANCER	TESTICULAR TORSION
SEXUAL DYSFUNCTION	UTERINE FIBROIDS
SPERMATOCELE	VAGINITIS
TESTICULAR CANCER	VULVODYNIA
TURNER'S SYNDROME	
UTERINE PROLAPSE	
VARICOCELE	

Traditions in Medical History

The high rate of maternal deaths from "childbirth FEVER" (puerperal fever) at the dawn of the era of antisepsis motivated Hungarian obstetrician Ignaz Philipp Semmelweis (1818–1861) to change his habits. In so doing, he transformed the practice of obstetrics and saved countless lives. By the middle of the 19th century scientists knew of the existence of microbes and their role in causing disease, though their mechanisms of infection remained a mystery. An emerging recognition was of the danger of infection for pathologists who performed autopsies. The slight wound from a slip of the scalpel was all too often fatal, causing systemic infection known as pathologist's pyemia. Semmelweis was the first to connect the two apparently

disparate conditions—puerperal fever and pathologist's pyemia—together.

Semmelweis practiced and taught at Vienna General Hospital, a major medical mecca of its time. Its maternity ward was very busy. As was the custom of the time, women attended by physicians went to one ward and women attended by midwives went to another ward. In 1847, the year of Semmelweis's epiphanic recognition, 20 to 35 percent of women who received care from doctors during childbirth died within weeks from puerperal fever. Only 2 percent of women who received their childbirth care from midwives met with similar fate.

Another customary practice of the time was for doctors to immediately autopsy patients who died, partly to provide education for student doctors. After his close friend died of a massive infection resulting from a wound suffered while conducting an autopsy, Semmelweis began to observe the patterns of illness in the maternity ward. He soon concluded that the practice of doctors freely moving between performing autopsies and attending to deliveries was the likely cause.

Semmelweis began to cleanse his hands with chlorinated lime before entering the childbirth ward and required his students to do the same. Though the caustic solution left the doctors' hands somewhat raw, nearly immediately the infection rate on their maternity ward dropped to 3 percent—much the same as the rate of infection on the midwifery ward. Midwives, of course, did not participate in autopsies. The change was a turning point in medicine's approach to childbirth. Within a decade antiseptics converged with the discovery of ANESTHESIA to vastly improve the safety and comfort of childbirth. When England's Queen Victoria received chloroform anesthesia during childbirth in 1853, she established a standard of acceptability for both improvements.

CESAREAN SECTION (surgical childbirth) also became a reasonable option for difficult deliveries, allowing doctors to save both mother and baby. Though ancient Chinese medical texts allude to a surgical childbirth procedure, cesarean section was an action of desperation to save the infant, generally carried out only when it was clear the mother had no chance of survival or had already died. Though popular mythology attributes the proce-

dure and its name to the surgical birth of Rome's Julius Caesar, most medical historians believe such a correlation is highly unlikely. More likely is the derivation of the name from the Latin word *caesones*, the term applied to the infants who survived surgical extraction from their dying or dead mothers. Historical records document that Julius Caesar's mother lived long after her son's birth.

Breakthrough Research and Treatment Advances

The final decades of the 20th century brought pivotal advances in reproductive medicine. The first in vitro fertilization (IVF) baby—"test tube baby"—was born in England in 1978. Since then ASSISTED REPRODUCTIVE TECHNOLOGY (ART) has brought thousands of babies into the world. Today IVF is the cornerstone of treatment for infertility. Nearly 45,000 ART babies are born in the United States each year.

The coupling of advances in diagnostic imaging procedures and surgical techniques gave birth to the new subspecialty of fetal surgery, in which surgeons can operate on the unborn fetus to correct potentially devastating or fatal birth defects such as severe SPINA BIFIDA and congenital diaphragmatic HERNIA (incomplete formation or absence of the DIAPHRAGM). Technologic advances have also vastly improved the survivability of premature (preterm) infants, with some measures targeting efforts to maintain the pregnancy as long as possible and others focused on supporting the still-developing baby after birth.

Among the flurry of advances in pharmaceuticals at the turn of the 21st century, none attracted quite so much attention or sales as the phosphodiesterase (PDE) inhibitor medication to treat ERECTILE DYSFUNCTION, sildenafil. The trade name product Viagra catapulted to record sales, becoming the highest selling DRUG of all time within six months of its release. Sildenafil was the first convenient treatment for physiologically based erectile dysfunction, which affects about 25 million men in the United States.

The start of the 21st century also marked the end of a more than 50-year tradition in medical history when extensive research studies concluded that routine hormone replacement therapy (HRT) to treat menopause did not provide the health benefits widely attributed to it but instead signifi-

cantly raised a woman's risk for certain cancers. As well, there was no evidence that HRT reduced a woman's risk for **CARDIOVASCULAR DISEASE (CVD)**, though supplemental estrogen did improve **BONE**

health and reduce **OSTEOPOROSIS**. However, new drugs are able to accomplish the same effect without the increased risk for cancer that comes with estrogen supplementation.



abortion The end of a PREGNANCY before the FETUS is viable (capable of independent life). Abortion may occur spontaneously (commonly called miscarriage) or be induced to end a pregnancy. In the United States, federal law mandates the availability of induced abortion, and state laws regulate the definition of viability as it applies to induced abortion. The range of legal viability is 20 weeks to 24 weeks of gestational age. The clinical border for viability is generally 20 weeks or a fetal weight of 500 grams (about 1 pound). It is uncommon for a fetus delivered between 24 and 20 weeks and unlikely for a fetus born before 20 weeks of gestational age to survive. A full-term pregnancy is 42 weeks.

Spontaneous Abortion

Numerous factors may initiate spontaneous abortion. The most vulnerable period of pregnancy for spontaneous abortion is between 7 and 12 weeks. Doctors believe that most abortions that occur within this early stage of pregnancy occur because the conceived EMBRYO has congenital or chromosomal defects that are not survivable. About 15 percent of known pregnancies end in spontaneous abortion before the 12th week of pregnancy. Regardless of the cause and the stage of pregnancy, spontaneous abortion is often a traumatic loss for the woman and her partner.

Induced Abortion

An induced abortion is a procedure a woman chooses to undergo to end a pregnancy and may be therapeutic (medically necessary for the woman's health or because the fetus has known, nonsurvivable defects such as anencephaly) or elective termination of pregnancy. An induced abortion may be a surgical procedure called dila-

tion and evacuation (D&E), performed under ANESTHESIA in a hospital operating room or in an AMBULATORY SURGICAL FACILITY, in which the doctor dilates the CERVIX and withdraws the contents of the UTERUS via suction (also called vacuum aspiration abortion). Before seven weeks an induced abortion may be a medical procedure, brought about by taking medications such as mifepristone (RU486), methotrexate, or misoprostol. These drugs, called abortifacients, prevent cell division (methotrexate, a CHEMOTHERAPY DRUG used to treat cancer) or implantation, or initiate uterine contractions (mifepristone and misoprostol).

Complications of Abortion

Uncontrolled bleeding (hemorrhage) and INFECTION are risks with either spontaneous or induced abortion. The abortion may be incomplete (some of the contents of CONCEPTION remain in the uterus), causing persistent or occasionally heavy bleeding. Persistent or heavy bleeding often requires DILATION AND CURETTAGE (D&C), a surgical procedure in which the doctor dilates the cervix and uses a curette to gently scrape the interior walls of the uterus. Undiagnosed GONORRHEA and CHLAMYDIA are the most common causes of postabortion infection. Infection requires treatment with ANTIBIOTIC MEDICATIONS. Either bleeding or infection may be life threatening; both require immediate medical evaluation and appropriate treatment. Rarely, abortion results in complications that can affect future FERTILITY.

Abortion, whether spontaneous or induced, is often an emotional experience for the woman and her partner. Guilt, sadness, and anger are common feelings that may persist for some time or reemerge years later. Induced abortion often has additional religious or philosophical implications.

See also BIRTH DEFECTS; [CHILDBIRTH](#); CHROMOSOMAL DISORDERS; [CONTRACEPTION](#); [ECTOPIC PREGNANCY](#); [FAMILY PLANNING](#); GENETIC DISORDERS; NEURAL TUBE DEFECTS; STILLBIRTH.

adenomyosis A condition in which the cells that make up the endometrium (the lining of the UTERUS) grow into the wall of the uterus (myometrium), forming benign (noncancerous) tumors that appear as thickenings or masses contained within the uterine wall. Adenomyosis nearly always occurs in women who have carried pregnancies to full term, causing doctors to believe the condition results from injury to the wall of the uterus as it stretches to accommodate the growth of the FETUS in the final weeks of PREGNANCY.

Adenomyosis may not cause symptoms; the doctor may discover its presence during evaluation for other health conditions affecting the uterus, such as DYSFUNCTIONAL UTERINE BLEEDING (DUB) or ENDOMETRIOSIS. The uterus may be tender to palpation (examination by touching) during PELVIC EXAMINATION. When symptoms do occur they may include PAIN during SEXUAL INTERCOURSE, unusually heavy menstrual bleeding, and intense menstrual cramping.

The diagnostic path may include ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, or MAGNETIC RESONANCE IMAGING (MRI), though definitive diagnosis requires myometrial biopsy (laboratory examination of a tissue sample from the uterine wall). The gynecologist may use HYSTEROSCOPY to obtain the biopsy, or may examine tissue obtained through procedures to treat DUB such as DILATION AND CURETTAGE (D&C).

The monthly surge of hormones that cause the endometrium to thicken is responsible for symptoms; the engorged endometrial tissue causes pressure where it has infiltrated the myometrium. Because this hormonal cycle ends with MENOPAUSE (cessation of the menstrual cycle), adenomyosis then goes away. Treatment thus attempts to relieve symptoms until menopause occurs and may include NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) or oral contraceptives (birth control pills) to regulate the hormonal balance that controls the MENSTRUAL CYCLE. When symptoms are severe and the woman does not desire further pregnancies, HYSTERECTOMY (surgery to remove the

uterus) may be a treatment option. Because the infiltration into the myometrium is diffuse (spread out), it is not possible to surgically remove only the sites of adenomyosis. Adenomyosis does not affect FERTILITY or the capability of the uterus to again expand in pregnancy.

See also [CONTRACEPTION](#); [DYSMENORRHEA](#); [ENDOMETRIAL CANCER](#); [ENDOMETRIOSIS](#); [UTERINE FIBROIDS](#).

adoption Accepting or relinquishing legal, social, and family responsibilities for a nonbiologic child. Adoption is an option within FAMILY PLANNING for people who desire children. Placing a child for adoption also an option in a circumstance of an unplanned PREGNANCY. About 150,000 adoptions take place in the United States each year. Adoptions may be open, in which there is direct or indirect contact between the biologic parents and the adoptive parents, or closed, in which the court seals the adoption records and biologic and adoptive parents do not know each other or anything about each other.

Each state in the United States has its own laws and procedures that regulate both sides of the adoption process. However, all states recognize and honor legal adoptions made in other states. Adoption laws regulate factors such as what information may be (or in some states, must be) made available to adult adopted children, the legal rights of biologic and adoptive parents, and the rights of biologic fathers who do not know their children were relinquished for adoption.

Countries around the world have their own laws and procedures for adoption that may or may not be consistent with practices in the United States. Though the United States generally recognizes foreign adoptions, federal immigration laws require specific evidence of legal adoption and other documentation. The US Department of State handles such matters. No matter the state or country, the legal issues of adoption are complex. It is prudent to obtain advice from a qualified adoption attorney before proceeding.

Health Concerns in Adopting a Child

Many adopted children come to their adoptive families with health concerns. Though it is ideal to have a full health history, including family history, for the adopted child, this does not often happen.

As a matter of course many adoptive families have the child undergo a comprehensive medical examination. Children adopted from other countries often have parasitic infections and other health conditions uncommon in the United States. FETAL ALCOHOL SYNDROME, congenital INFECTION with SEXUALLY TRANSMITTED DISEASES (STDs), HEPATITIS, RICKETS, TUBERCULOSIS, and hearing loss and VISION IMPAIRMENT are also common, especially with international adoptions. Though these are often treatable conditions, they do require prompt medical attention. Children older than one year may have emotional and psychologic problems as well. Sometimes, even in a closed adoption, the intermediary (adoption agency or attorney) is able to obtain more specific health information about the child to pass onto the adoptive parents. Conditions that require ongoing care, such as fetal ALCOHOL syndrome or developmental disabilities, are special needs.

Placing a Child for Adoption

Women have varying and often deeply personal reasons for placing their biologic children for adoption. Common reasons for being unable to retain parental rights include

- serious DRUG or alcohol abuse problems
- extreme youth or immaturity
- pregnancy that was the result of rape or incest
- health or disability issues that prohibit properly caring for a child

As well, mothers sometimes abandon their children without known reason. A woman who desires to place her child for adoption can notify her doctor, a community service agency, an adoption service, or an attorney. Typically there are no expenses to the relinquishing parent. Depending on circumstances the biologic mother may choose the adoptive family, especially if she is pregnant at the time she makes the decision to place the child for adoption.

The decision to place a child for adoption, which on the surface may appear straightforward, has lifelong emotional consequences for mother and child. The mother may feel guilty for “giving up” her child. The child, when old enough to understand what adoption means, may feel aban-

doned regardless of the circumstances of the adoptive family. It is important for adoptive families to be loving yet as open as possible about questions adoptive children may ask. Many communities have SUPPORT GROUPS for adoptive parents, adopted children, and people who placed their children for adoption. Support groups can help people share their concerns, feelings, and solutions to common problems.

Parenting and family are life experiences that have challenges and accomplishments, perils and joys, no matter what their configurations. For many adults who adopt, adoption brings to fruition a lifelong dream to raise and parent a child, either starting or adding to a family. And for many children who are adopted, adoption is daily evidence that someone wants them and loves them very much.

See also CULTURAL AND ETHNIC HEALTH CARE PERSPECTIVES; [GESTATIONAL SURROGACY](#); PARENTING.

aging, reproductive and sexual changes that occur with The reproductive system, male or female, is intact but immature at birth and remains immature until the onset of PUBERTY around age 12. Researchers do not know what triggers the physiologic events that take place to initiate reproductive and sexual maturity. However, these events result in the development of SECONDARY SEXUAL CHARACTERISTICS, sex drive and interest, and the ability to produce new life. Male FERTILITY extends from puberty to the end of life, though may diminish somewhat in late old age. Female fertility is finite, starting at MENARCHE (the onset of the MENSTRUAL CYCLE) and ending with MENOPAUSE (the conclusion of the menstrual cycle). Only for a few days each month is a woman capable of CONCEPTION.

The hormones of sexual and reproductive maturity have numerous and far-reaching effects in the body. Men and women alike have the spectrum of sex hormones: ESTROGENS and ANDROGENS. Androgens dominate in men; estrogens dominate in women. These hormones account for secondary sexual characteristics and reproductive ability as well as MUSCLE mass and STRENGTH, BONE DENSITY, lipid metabolism, aspects of cardiovascular function, cognitive clarity, BRAIN function, mood, and emotion.

Age-related hormonal changes are most prominent in women, who experience significant transformation in their bodies with menopause. The cessation of OVULATION means a pronounced drop in estrogen within the body, affecting not only reproductive capability but also the functions of nearly every system in the body. Health concerns that arise from these changes include increased risk for OSTEOPOROSIS, CARDIOVASCULAR DISEASE (CVD), and certain types of cancer. Men also experience age-related changes in sexuality and reproductive function. A man's testosterone level peaks when he is in his early 20s and gradually declines with each decade of life. By age 60 most men have about half the testosterone they had at age 25. This decline results in changes such as diminished muscle mass and strength and male pattern baldness (ALOPECIA). A man's risk for PROSTATE CANCER significantly increases after age 60. Though a man can still father children even into his 80s, declining testosterone affects LIBIDO (sex drive) and erectile function.

See also ANDROPAUSE; BENIGN PROSTATIC HYPERPLASIA (BPH); ERECTILE DYSFUNCTION; LIFESTYLE AND HEALTH; MENSTRUATION; PROGESTERONE.

alpha fetoprotein (AFP) A protein the LIVER produces. In PREGNANCY the amount of AFP in the woman's BLOOD circulation increases, reflecting the activity of the FETUS's liver as it develops and becomes functional. A blood test measures AFP in the woman's blood circulation early in the second trimester, between 15 and 22 weeks of pregnancy.

Elevated AFP levels in pregnancy may indicate a multiple pregnancy, NEURAL TUBE DEFECTS or defects in the structure of the abdominal wall that allow the organs of the gastrointestinal system to form outside the body. Chronic liver disease, such as HEPATITIS or CIRRHOSIS, also elevates AFP. Excessive ALCOHOL consumption and cigarette smoking are common causes of falsely high measures. Low AFP levels may indicate a pregnancy that is not as advanced as the woman believes or suggest the chromosomal disorder DOWN SYNDROME.

Other health circumstances elevate AFP blood levels in nonpregnant women and in men. Among them are liver disease, including LIVER CANCER, TESTICULAR CANCER in men, and OVARIAN CANCER in women. Deviations from normal AFP levels in

pregnancy suggest circumstances that may warrant further medical evaluation such as ULTRASOUND, AMNIOCENTESIS, and CHORIONIC VILLI SAMPLING (CVS).

See also ALCOHOLISM; CHROMOSOMAL DISORDERS; GENETIC DISORDERS; [PRENATAL CARE](#).

amenorrhea The absence of menstrual periods. Primary amenorrhea occurs when a young woman does not begin menstruating by age 16; secondary amenorrhea occurs in women who have been menstruating and then stop (miss six or more consecutive periods).

Primary amenorrhea may result from GENETIC DISORDERS such as TURNER'S SYNDROME or from hormonal disorders such as pituitary ADENOMA (a tumor of the PITUITARY GLAND) or HYPOTHYROIDISM (underactive THYROID GLAND). PREGNANCY is the most common cause of secondary amenorrhea. Other factors that may cause either primary or secondary amenorrhea include intense physical exercise, excessive body weight (OBESITY), and extreme underweight such as may result from EATING DISORDERS.

Amenorrhea is a symptom of underlying conditions that affect the function of the OVARIES rather than itself a health condition. Because the hormones the ovaries produce affect many other functions within the body, it is important to identify its cause. Unresolved primary amenorrhea may have consequences such as permanent INFERTILITY and failure to develop SECONDARY SEXUAL CHARACTERISTICS.

See also BODY MASS INDEX (BMI); [DYSMENORRHEA](#); EXERCISE AND HEALTH; [FERTILITY](#); [HORMONE](#); OBESITY AND HEALTH; [OVULATION](#); PRIMARY OVARIAN FAILURE; WEIGHT LOSS AND WEIGHT MANAGEMENT.

amniocentesis A diagnostic procedure to withdraw a sample of AMNIOTIC FLUID from the UTERUS of a pregnant woman to obtain information about the health status of the FETUS. Obstetricians use amniocentesis, typically performed during the second trimester of PREGNANCY, to help diagnose GENETIC DISORDERS and health conditions of the developing fetus such as DOWN SYNDROME or SPINA BIFIDA and other NEURAL TUBE DEFECTS. Amniotic fluid contains cells from the fetus that can provide a KARYOTYPE (representation of CHROMOSOME pair-

ings) and other genetic information about the fetus. The amniotic fluid may also provide information about the woman's health, such as whether any INFECTION is present, and help doctors determine whether the fetus's lungs are mature.

To perform amniocentesis, the obstetrician first numbs a small area on the surface of the woman's abdomen, either with a topical anesthetic spray or an injection of local anesthetic. The obstetrician then inserts a long needle through the woman's abdominal wall into the amniotic sac and withdraws about 20 milliliters (less than an ounce) of amniotic fluid for laboratory analysis. ULTRASOUND helps determine the position of the fetus and the ideal insertion and placement of the needle so as to avoid injury to the fetus. Because the laboratory must first cultivate cells from the amniotic fluid, GENETIC TESTING results take two to three weeks.

Risks of amniocentesis include bleeding, infection, injury to the fetus, and spontaneous ABORTION (loss of the pregnancy). Some women feel temporary discomfort during the procedure, and many women find the requisite full BLADDER (necessary for the ultrasound) causes pressure and other discomforts. Some women experience mild cramping and slight bleeding for a day or two after the amniocentesis.

See also ALPHA FETOPROTEIN (AFP); ANESTHESIA; CHORIONIC VILLI SAMPLING (CVS); CHROMOSOMAL DISORDERS; CONGENITAL ANOMALY; PRENATAL CARE.

amniotic fluid The liquid that surrounds the developing FETUS within the amniotic sac, a membranous structure that forms inside the UTERUS in PREGNANCY. The amnion, the inner membrane of the amniotic sac, begins producing amniotic fluid at about two weeks of gestation. The amniotic fluid, which is mostly water, cushions the fetus against changes in temperature as well as jarring and bumps from outside the womb. The composition of amniotic fluid changes somewhat over the duration of pregnancy though typically includes, in addition to water, electrolytes, lipids, proteins, metabolic byproducts, and cells that the fetus sheds. These cells provide the DNA that AMNIOCENTESIS uses to assess the health of the fetus.

Amniotic fluid is essential not only to protect the fetus but also for proper fetal development. In

the second trimester the fetus swallows and "breathes" to take amniotic fluid into its STOMACH and LUNGS, which is necessary for development of the structures and functions of the pulmonary and gastrointestinal systems. The fetus also begins contributing URINE to the composition of the amniotic fluid. By the third trimester the amniotic fluid replenishes itself about every three hours and reaches a volume of approximately 500 milliliters. The amniotic sac ruptures when CHILDBIRTH is imminent, sending a flood of amniotic fluid from the woman's VAGINA. This process is the "breaking water" that often heralds the onset of pregnancy's final stages, labor and delivery.

A lower than normal volume of amniotic fluid is oligohydramnios, which may constrict the movement of the fetus to an extent that causes abnormal musculoskeletal development, intra-uterine growth retardation, and other problems. A greater than normal volume of amniotic fluid is polyhydramnios, which may indicate NEURAL TUBE DEFECTS OR BIRTH DEFECTS of the KIDNEYS or gastrointestinal structures. Polyhydramnios is sometimes present when the mother has diabetes. It presents increased risk for UMBILICAL CORD problems such as umbilical cord prolapse (the umbilical cord enters the vagina before the fetus's head as birth begins, a potentially life-threatening scenario for the fetus), as well as large for gestational age or macrosomia (birth weight significantly higher than normal).

For further discussion of amniotic fluid within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also CESAREAN SECTION.

andropause A term sometimes used to describe the physical and emotional changes men experience at midlife. The amount of TESTOSTERONE, the primary male sex HORMONE, in a man's BLOOD circulation begins to slowly and steadily decline after reaching its peak in the early to middle 20s. By age 75, testosterone levels are typically about half of what they were at age 25. Though this is still an adequate level of testosterone to maintain masculinity, the decline accounts for some of the physical changes characteristic of midlife in men: conversion of MUSCLE to fat, redistribution of body

fat, and sometimes diminished energy and LIBIDO (sex drive). Some men experience clinical DEPRESSION, loss of BONE mass, ERECTILE DYSFUNCTION, and other symptoms as a consequence of lower testosterone levels. Some researchers believe the decline in testosterone levels contributes to the increased risk for HEART ATTACK as a man gets older.

Doctors may recommend prescription hormone supplementation with ANDROGENS (testosterone or testosterone precursors) for men who have unacceptable symptoms. However, the long-term therapeutic value and possible risks of such treatment remain uncertain. Some men take the over-the-counter product DEHYDROEPIANDROSTERONE (DHEA), available in the United States as a dietary supplement, as an androgen precursor (a substance the body converts to testosterone during its METABOLISM). There are few clinical studies to provide clear evidence of whether this is effective or safe. Some doctors believe as long as the DHEA does not push testosterone levels beyond the normal range, the risk for adverse health effects is minimal. However, other doctors worry that sustained increases in blood testosterone levels in men over age 50 may increase the risk for PROSTATE CANCER and CARDIOVASCULAR DISEASE (CVD).

See also ADRENAL INSUFFICIENCY; AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; ANABOLIC STEROIDS AND STEROID PRECURSORS; HORMONE-DRIVEN CANCERS; MENOPAUSE.

Apgar score A standardized measure of an infant's health status, typically assessed one

minute and five minutes after birth. Anesthesiologist Virginia Apgar (1909–1974) developed the scoring system that bears her name in 1953, assigning a point value of 0, 1, or 2 to each of five categories of vital function (BREATHING, HEART RATE, REFLEX response, MUSCLE tone, and SKIN color) and reporting their sum as the overall Apgar score. Today the Apgar score is an international standard to assess whether a newborn needs resuscitation (lifesaving measures) and to evaluate the success of resuscitative efforts. The highest score possible is 10; doctors consider a score between 7 and 10 to reflect good health in the infant. A score between 4 and 7 bears monitoring and perhaps supportive care such as suctioning of the airways or supplemental oxygen. A score of 3 or lower indicates a life-threatening or critical circumstance for the infant.

See also [CHILDBIRTH](#); [PREMATURE BIRTH](#).

assisted reproductive technology (ART) Medical interventions to produce PREGNANCY. The US Centers for Disease Control and Prevention (CDC), which has a mandate under federal law to report the success rates of ART at FERTILITY clinics in the United States each year, defines ART as any method that involves manipulation of both SPERM and OVA (eggs). Other methods to aid fertility may use interventions such as HORMONE therapies to stimulate OVULATION (the release of ova) in the woman or techniques such as intrauterine artificial insemination (placement of sperm within the UTERUS) to improve sperm viability. ART typically

APGAR SCORES			
Apgar Score	0	1	2
BREATHING	not breathing	slow or irregular breathing	20 to 50 breaths per minute, regular rhythm
HEART RATE	no heart rate	< 100 beats per minute	100 to 104 beats per minute
REFLEX response	no response to nasal stimulation	facial grimace with nasal stimulation	sneeze or cough with nasal stimulation
MUSCLE tone	flaccid	some flexing of the arms and legs	active movement
SKIN color	cyanotic (bluish gray)	cyanotic limbs	pink

becomes an option to treat INFERTILITY when less invasive approaches fail to result in pregnancy or when health factors compromise fertility in both partners.

Methods of ART

Most methods of ART involve uniting sperm and ova outside the body and returning the results to the woman's body. There are four commonly used methods of ART:

- In vitro fertilization (IVF) is the most common method of ART. The technologist mixes sperm and several ova together in a laboratory container. The sperm penetrate and fertilize the ova. After the zygotes form, the fertility specialist transfers two to four zygotes into the woman's uterus. IVF eliminates issues of sperm motility, sperm antibodies, and blocked FALLOPIAN TUBES. It may be an appropriate choice for male factor infertility, female factor infertility, or combined factor infertility and may use donor eggs, donor sperm, or eggs and sperm collected from the woman and her partner.
- GAMETE intrafallopian transfer (GIFT) mixes ova and sperm in a thin catheter and transfers the mixture directly to the woman's fallopian tube. Fertilization takes place within the fallopian tube and the ZYGOTE travels to the uterus to implant. GIFT may be the ART method of choice when the woman has healthy fallopian tubes and male factor infertility is the primary issue. GIFT is also an acceptable method of assisted CONCEPTION within cultures and belief systems in which fertilization must take place inside the woman's body.
- Intracytoplasmic sperm injection (ICSI) is somewhat like IVF though leaves less to chance. The technologist extracts a single sperm from the collected sperm and injects it into an ovum to fertilize the ovum. The fertility specialist then transfers the zygote into the woman's fallopian tube or uterus. ICSI is often the ART method of choice for male factor infertility, especially when the man's sperm count is very low.
- Zygote intrafallopian transfer (ZIFT) begins with IVF though the fertility specialist then

uses laparoscopy to place two to four zygotes into the woman's fallopian tube. ZIFT is a common ART choice for male factor infertility and may be appropriate when IVF has not succeeded. Fertility specialists believe the embryos that result from IVF may be more fragile than those that develop within the fallopian tube.

Before any of these methods can occur, the fertility clinic must obtain ova and sperm, either from the woman and man undergoing ART or from donors. Ova retrieval begins with injection of a hormone, human chorionic gonadotropin (hCG). Then, 36 hours later, the fertility specialist aspirates (gently suctions away) the ripened ova using a catheter inserted into the pelvic cavity through the vagina with ULTRASOUND to visualize and guide the process. Sperm retrieval may occur through EJACULATION or the fertility specialist may extract sperm, using needle and syringe, directly from the man's testicle (EPIDIDYMIS). Sperm extraction does not require hormones.

Success of ART

About 45,000 births occur in the United States each year as a result of ART, representing about a 25 percent success rate overall for ART. However, many couples undergo multiple ART attempts, and the rate of pregnancy correlates to the woman's age with a precipitous drop after age 35. Nearly a third of ART conceptions are multiples (twins or higher), a consequence of the practice of implanting multiple embryos to improve the likelihood of a viable pregnancy (pregnancy that carries to full term with delivery of a healthy baby). Some ART methods are more successful than others, depending on the infertility circumstances. As well, the ART may succeed in generating a pregnancy but the pregnancy does not carry to term. The CDC reports annual ART success rates for pregnancies and live births according to ART method and by fertility center. The report is available at the CDC's Web site (www.cdc.gov/art).

Concerns and Risks of ART

Despite significant advances in understanding and technology, much about fertility remains a mystery. The long-term risk associated with hormone use to stimulate ovulation for egg retrieval in

women is probably negligible but remains unknown. Risks for chromosomal and genetic damage also remain unknown. However, since the first successful IVF in 1978, hundreds of thousands of babies born through ART methods have reached adulthood and many now have children of their own with both parent and child healthy. It

is important for people considering ART to know as much as possible about their family health histories and to fully understand the possible complications and risks for the methods of ART they are considering, because knowledge in this area changes rapidly.

See also [ADOPTION](#); [FAMILY PLANNING](#).

B

balanitis INFLAMMATION of the glans, the tip of the PENIS, usually the consequence of a bacterial or fungal (yeast) INFECTION. Balanitis is more likely to occur in uncircumcised men, as the foreskin can provide the moist, warm environment that supports the growth of pathogens. Diligent PERSONAL HYGIENE is especially important in uncircumcised men to keep the area beneath the foreskin clean and dry to prevent irritation and infection. The diagnostic path may include laboratory culture of a sample swabbed from the inflamed area to determine the cause of the infection, with appropriate ANTIBIOTIC MEDICATIONS OR ANTIFUNGAL MEDICATIONS to treat the infection. Medications may be oral (taken by MOUTH), topical (applied to the penis), or both.

Most balanitis clears with treatment and hygienic measures. A potentially serious complication is PHIMOSIS, in which the foreskin forms adhesions to the glans and becomes unretractable. Phimosis further complicates balanitis and may require CIRCUMCISION (surgical removal of the foreskin).

See also BACTERIA; CANDIDIASIS; CHLAMYDIA; FUNGUS; HUMAN PAPILLOMAVIRUS (HPV); PATHOGEN; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION.

Bartholin's cyst A fluid-filled enlargement of a Bartholin's gland. There are two Bartholin's glands, one on each side of the entrance to the VAGINA. Normally undetectable, the Bartholin's glands produce secretions that lubricate the vaginal opening. A cyst may form when the duct that allows the secretions to drain from the gland becomes blocked (occluded). The secretions continue to accumulate but have no exit, causing the gland to gradually enlarge. The enlargement may become quite large before a woman can detect it,

and often causes no symptoms until its size causes discomfort.

The gynecologist can diagnose a Bartholin's cyst on the basis of its appearance. Treatment is to drain the cyst, after which the gland returns to normal function. The gynecologist may place a tiny tube temporarily into the cyst to allow the accumulated fluid to drain, or may make a small incision to release the fluid, then suture the incision open to maintain drainage. These procedures are usually performed in the gynecologist's office with local ANESTHESIA to first numb the area. Occasionally an INFECTION develops within a Bartholin's cyst, which requires a course of treatment with ANTIBIOTIC MEDICATIONS.

See also VAGINITIS.

benign prostatic hyperplasia (BPH) A non-cancerous enlargement, also called benign prostatic hypertrophy, of a man's PROSTATE GLAND. BPH is common in men over age 60 and is a condition of aging. Though BPH is not cancer, some men who have BPH do develop PROSTATE CANCER. Researchers do not know what causes BPH though believe the changes in HORMONE levels and ratios that naturally occur with aging probably are key.

BPH develops when the number of cells in the prostate gland increases, causing the gland to grow. The prostate gland encircles the URETHRA like a cuff at the neck of the BLADDER. BPH typically constricts the urethra, either by compressing it from the outside or blocking it from the inside if prostate cells invade the urethral walls. The resulting occlusion interferes with URINATION.

Symptoms and Diagnostic Path

The symptoms of BPH develop gradually over time and may include

- hesitation when urinating (stopping and starting during the flow)
- URINARY URGENCY and URINARY FREQUENCY, especially at night (NOCTURIA)
- dribbling URINE after the man finishes urinating
- HEMATURIA (bloody urine)
- URINARY INCONTINENCE

The diagnostic path includes a BLOOD test to measure the PROSTATE-SPECIFIC ANTIGEN (PSA) level and a DIGITAL RECTAL EXAMINATION (DRE), which allows the doctor to palpate (feel) the prostate gland through the wall of the RECTUM. This examination helps determine whether the enlargement of the prostate gland is likely benign (the gland feels soft to palpation) or suspicious (the gland feels hard or irregular). Further diagnostic procedures may include measurement of postvoiding urine (urine that remains in the bladder after urination), ULTRASOUND of the bladder, and occasionally CYSTOURETHROGRAM to rule out other causes of the symptoms.

Treatment Options and Outlook

Treatment depends on the nature of the prostate gland's overgrowth, the severity of symptoms, and the man's preferences. Treatment options include

- MINIMALLY INVASIVE SURGERY to remove excess prostate gland tissue
- transurethral resection of the prostate (TURP), an OPERATION in which the urologist removes portions of the prostate gland using an endoscopic instrument inserted through the urethra
- PROSTATECTOMY, an operation to entirely remove the prostate gland
- alpha blocker medications, which relax smooth MUSCLE tissue to improve the flow of urine
- 5-alpha reductase inhibitor medications such as finasteride and dutasteride, which block the conversion of TESTOSTERONE to dihydrotestosterone (DHT) to slow the growth of prostate gland cells
- herbal remedies such as SAW PALMETTO, stinging nettle extract, SOY protein and soybean products, and flaxseed oil

MEDICATIONS TO TREAT
BENIGN PROSTATIC HYPERPLASIA (BPH)

alfuzosin	doxazosin
dutasteride	finasteride
prazosin	tamsulosin
terazosin	

Prostatectomy is the only cure for BPH, though it has significant risks and potential complications. Most men are able to achieve long-term relief of symptoms through medication or minimally invasive procedures.

Risk Factors and Preventive Measures

Age is the primary risk factor for BPH. BPH is rare in men under age 50 and nearly always present in men over age 70. There are no known methods for preventing BPH. It is important for men over age 50 to undergo recommended preventive screening and examination for prostate cancer, as the risk for prostate cancer also increases with age and its early symptoms are indistinguishable from those of BPH.

See also AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; BLADDER CANCER; ENDOSCOPY; HORMONE-DRIVEN CANCERS; SURGERY BENEFIT AND RISK ASSESSMENT; URETHRAL STRICTURE.

birth control See CONTRACEPTION.

breast The mammary gland. Both men and women have breasts. Each person's two breasts are close to but not exactly the same size and shape. Breasts vary widely in appearance among both men and women.

At PUBERTY the female sex hormones (primarily ESTROGENS) in girls cause the glandular components of the breast to enlarge, establishing the potential to produce milk. The nipple also enlarges as does the glandular tissue surrounding it, the areola. Enlarged breasts are among the female SECONDARY SEXUAL CHARACTERISTICS. Female breasts fill out with adipose (fatty) tissue and connective tissue in addition to its glandular structures, becoming rounded, and extend out from the chest. The male sex hormones (primarily TESTOSTERONE) have the opposite effect in boys, causing the glandular components to all but disappear. In adulthood the male breasts remain relatively flat against the chest.

The glandular components of the adult female breast are the lactiferous glands, which can produce and secrete milk, and the lactiferous ducts, which store milk. Fatty tissue accumulates around these structures, called lobules. Supportive connective fibers called Cooper ligaments group the lobules into lobes. Each breast contains between 15 and 20 lobes. Milk production, called lactation, occurs under the stimulation of PROLACTIN, a HORMONE the PITUITARY GLAND begins to secrete after CHILDBIRTH. Lactation may continue for as long as the woman continues BREASTFEEDING. Another hormone, OXYTOCIN, stimulates the release of milk from the breast. The breasts may become significantly larger (up to three times their prepregnancy size) while the woman is breastfeeding. When breastfeeding stops the lactiferous structures (glands and ducts) shrink and the breasts return to their normal size.

The breasts are also sources of sexual stimulation and arousal for women and for men, both by touch and visually. During sexual arousal and at ORGASM the nipples become firm and erect. A woman's breasts may become uncomfortably tender and sometimes swollen during the luteal phase of the MENSTRUAL CYCLE, in response to the elevation of estrogens in the BLOOD circulation.

At MENOPAUSE the glandular tissue in the breast shrinks and the breast structure becomes much less dense. At this time a woman's risk for BREAST CANCER increases significantly. Current preventive health guidelines recommend routine MAMMOGRAM (X-RAY of the breast) beginning at age 40 for most women, and beginning earlier and occurring more frequently in women who have high risk for developing breast cancer. Health experts recommend that all women, beginning at the conclusion of puberty, perform monthly BREAST SELF-EXAMINATION as a method of early detection for BREAST HEALTH concerns, including lumps that may be cancerous.

HEALTH CONDITIONS THAT CAN AFFECT THE BREASTS

BREAST CANCER	fibroadenoma
FIBROCYSTIC BREAST DISEASE	GYNECOMASTIA
INTRADUCTAL PAPILLOMA	MASTALGIA
MASTITIS	PAGET'S DISEASE OF THE BREAST

For further discussion of the breast within the context of the structures and functions of repro-

duction and sexuality, please see the overview section "The Reproductive System."

See also LIGAMENT; PREMENSTRUAL SYNDROME (PMS); TURNER'S SYNDROME.

breast cancer A malignant (cancerous) tumor that arises in the BREAST. There are many types of breast cancers, some of which are HORMONE driven (draw sustenance from ESTROGENS or PROGESTERONE) and others that are not. Primary breast cancer originates in the breast; secondary breast cancer metastasizes (spreads) to the breast from an origin elsewhere in the body. Breast cancer may also metastasize to other sites in the body such as the LUNGS or bones.

Breast cancer is the most common cancer among American women; doctors in the United States diagnose breast cancer in about 200,000 women each year. Breast cancer is currently second to LUNG CANCER as the leading cause of deaths due to cancer among women. However, significant advances in the early 2000s in understanding the mechanisms of breast cancer cells and the resulting development of new treatments are changing the landscape of breast cancer.

Genetic factors The genes BRCA-1/BRCA-2 were the first genes conclusively linked to cancer. Inherited mutations in these genes significantly increase a woman's risk for breast cancer and OVARIAN CANCER. Researchers continue to study these mutations for ways to take advantage of them for preventing or treating cancers in women who have either or both mutations.

Other mutations are not hereditary but instead occur over time, the consequence of molecular damage that becomes cumulative over time. Researchers have identified nearly two dozen genes that influence cell proliferation (cell growth and division) in some way. One of the most significant is the *her-2* GENE (human epidermal growth factor receptor 2, also called HER-2/neu) gene, located on CHROMOSOME 17. The *her-2* gene expresses (directs the production of) certain protein receptors on the surfaces of cell membranes. The receptors allow binding with the HER-2/neu protein, a protein that instructs the cell to grow and divide. Mutations in the *her-2* gene cause increased numbers of HER-2/neu receptors on cells, allowing greater HER-2/neu binding. This

process, called overexpression, alters the way in which the cells grow and divide.

Hormonal factors Breast cancer cells may have receptors on the surfaces of their cell membranes for estrogen, progesterone, or both. These are hormone-positive cancer cells—designated as estrogen positive (ER+) or progesterone positive (PR+), with an accompanying percentage or numeric value that identifies the relative proportion or number of positive hormone receptors.

Immune factors The risk for breast cancer, like most types of cancer, increases with age. As immune function diminishes with age, so does the body’s ability to protect itself against health conditions such as cancer. Researchers are exploring the roles foods and NUTRIENTS play in supporting the IMMUNE SYSTEM’S ability to identify, contain, and eliminate cancer cells that develop. Immune dysfunction appears to play a direct role in one rare but aggressive type of breast cancer, inflammatory breast cancer (IBC). In IBC the breast cancer cells collect in the LYMPH vessels, causing INFLAMMATION within the breast rather than forming a discreet tumor.

TYPES OF BREAST CANCER

ADENOCARCINOMA	infiltrating comedocarcinoma
infiltrating intraductal	infiltrating lobular carcinoma
CARCINOMA (IDC)	inflammatory BREAST cancer
intraductal carcinoma	(IBC)
lobular carcinoma in situ	mucinous (colloid) carcinoma
(LCIS)	noninfiltrating
noninfiltrating intraductal	comedocarcinoma
carcinoma	PAGET’S DISEASE OF THE BREAST
papillary carcinoma	tubular carcinoma

Breast cancer in men Though people think of breast cancer as a woman’s condition, men also can develop breast cancer. Breast cancer in men is rare, occurring in 1 man for every 100 women who develop it. Men develop fewer types of breast cancers as well, because their breasts do not have the glandular tissue prevalent in the breasts of women. The types of breast cancers that occur in men are ADENOCARCINOMA, ductal carcinoma in situ (DCIS), and infiltrating ductal carcinoma (IDC). Men can also develop PAGET’S DISEASE OF THE BREAST, a condition in which cancer cells migrate into the SKIN around the nipple, though this

uncommon type of cancer is even more rare in men than in women. Symptoms of male breast cancer are the same as symptoms breast cancer in women. Many treatment options are also the same. Doctors diagnose about 1,700 men with breast cancer each year in the United States.

Symptoms and Diagnostic Path

In most situations the only symptom of breast cancer is a lump that the woman, her health-care provider, or a mammogram detects. Most breast cancer tumors do not hurt. Other symptoms of breast cancer may include

- nipple discharge, typically watery or sometimes blood tinged
- dimpling of the skin on the surface of the breast
- changes in the appearance of, or inversion of, the nipple
- changes in the shape or profile of the breast
- general sense of tiredness or lack of energy

The diagnostic path may include diagnostic mammogram, breast ULTRASOUND, fine-needle aspiration biopsy of the lump to obtain cell samples for laboratory examination, or excisional biopsy to remove the lump and provide tissue for laboratory examination. Excisional biopsy provides conclusive diagnosis. The pathologist determines the hormonal sensitivity of the cancer cells (estrogen or progesterone receptor positive) and whether they are *her-2* positive or negative. Many cancer centers conduct further testing to analyze the genetic composition of the cancer cells. Such testing provides insights into how the cancer cells grow and often reveals their vulnerabilities, allowing precisely targeted treatments. As well, the pathologist evaluates the size and characteristics of the tumor to determine its grade (level of abnormality in the cells) and stage (extent of the tumor). These factors in combination are crucial for determining appropriate CANCER TREATMENT OPTIONS AND DECISIONS.

Treatment Options and Outlook

Primary treatment for early stage breast cancer of any type is surgery to remove the cancer, which may be lumpectomy (removal of the lump and a

safe margin of normal tissue), segmental MASTECTOMY (removal of the one quarter segment of the breast that contains the tumor), simple mastectomy (removal of the breast), or modified radical mastectomy (removal of the breast and some surrounding tissue along with SENTINEL LYMPH NODE DISSECTION).

Nearly all women who have surgery for breast cancer also receive adjuvant (follow-up) therapy, which may include RADIATION THERAPY, CHEMOTHERAPY, HORMONE THERAPY, OR MONOCLONAL ANTIBODIES (MABS) therapy, either singularly or in combination. These therapies also may be primary treatment for later stage and recurrent breast cancers. In the late 1990s hormone therapy and MAb therapy (also called biological response modifier therapy or IMMUNOTHERAPY) became the frontrunners in adjuvant therapy for HORMONE-DRIVEN CANCERS—tumors sensitive to estrogen (ER+) or progesterone (PR+)—and HER-2/neu-positive tumors, respectively. In late 2005 the National Comprehensive Cancer Network (NCCN) issued revised treatment guidelines for breast cancer in which the cancer's hormone and *her-2* status are the primary factors for deciding the type and course of adjuvant therapy, with the traditional practice of evaluating tumor size and the degree of METASTASIS being a secondary step.

Hormone therapy for breast cancer Hormone therapy targets suppression of estrogen and progesterone in the woman's body. Among the therapies to achieve this goal are

- selective estrogen receptor modulators (SERMs), drugs that bind with estrogen receptors to keep estrogen from doing so; SERMs have some estrogen-like qualities that help maintain BONE DENSITY and lipid METABOLISM
- estrogen receptor downregulators (ERDs), which first bind with estrogen receptors and then destroy them
- aromatase inhibitors, which block the action of aromatase, an enzyme that converts ANDROGENS naturally occurring in body tissues such as fat into estrogen

Hormone therapy for breast cancer is effective in women who are past MENOPAUSE or who have no ovarian function due to surgical removal of the

OVARIES (OOPHORECTOMY) or chemical suppression of ovarian function (medications such as goserelin and leuprolide). Blocking estrogen production cuts off the supply of estrogen to cancer cells that require it, preventing the cells from growing. Side effects that may occur with hormone therapy include JOINT PAIN, NAUSEA, DIARRHEA, HEADACHE, and HOT FLASHES.

SERMs were the first effective hormone therapy drugs (tamoxifen came on the market in the 1980s). They generally have therapeutic value for about five years, after which their ability to bind with estrogen receptors diminishes. Oncologists may recommend taking a SERM for five years and then switching to an aromatase inhibitor, which does not appear to have time-limited usefulness. Aromatase inhibitors and ERDs are too new in clinical practice to know their long-term effectiveness.

HORMONE THERAPY DRUGS TO TREAT BREAST CANCER

Selective Estrogen Receptor Modulators (SERMs)

raloxifene (Evista)
tamoxifen (Nolvadex)
toremifene (Fareston)

Aromatase Inhibitors

anastrozole (Arimidex)
exemestane (Aromasin)
letrozole (Femara)

Estrogen Receptor Downregulators (ERDs)

fulvestrant (Faslodex)

Trastuzumab (Herceptin) Trastuzumab, a monoclonal antibody, specifically targets *her-2* receptors on breast cancer cells. First produced in the early 1970s, trastuzumab demonstrated its effectiveness against *her-2* positive breast cancer in the 1980s and became the cornerstone of treatment for *her-2* positive metastatic breast cancer in the 1990s. Because trastuzumab so narrowly targets breast cancer cells, it causes few side effects. However, one significant, though rare, SIDE EFFECT is HEART FAILURE. In the first decade of the 2000s, oncologists began administering trastuzumab for *her-2* positive stage 2, stage 3, and stage 4/metastatic breast cancers along with combination chemotherapy.

CHEMOTHERAPY AGENTS TO TREAT BREAST CANCER

capecitabine	cyclophosphamide
docetaxel	doxorubicin
epirubicin	5-fluorouracil (5FU)
gemcitabine	paclitaxel
vinorelbine	

Risk Factors and Preventive Measures

Age is the primary risk factor for breast cancers of all types, with the likelihood of developing breast cancer reaching one in two for women 85 and older. Hereditary factors (such as BRCA-1/BRCA-2) influence about 5 percent of breast cancers. Lifestyle factors that contribute to nonhereditary breast cancers include EATING HABITS that feature high-fat foods, lack of physical exercise, cigarette smoking, and excessive ALCOHOL consumption.

There is a strong correlation between OBESITY and breast cancer, though researchers do not know whether this is a circumstance of excess body fat or the consequence of eating habits and physical inactivity. Fat cells convert androgens to estrogen, raising the level of estrogens in the blood circulation. Continued exposure to elevated levels of estrogen is a risk factor for breast cancer as well as other hormone-driven cancers.

It is not possible at present to completely prevent breast cancer. However, lifestyle improvements can significantly reduce the risk of developing breast cancer. Regular breast examination from a health care provider, breast self-examination, and mammograms make possible early detection of breast cancer, which establishes the most ideal circumstances for successful treatment.

See also CANCER PREVENTION; DIET AND HEALTH; FIBROCYSTIC BREAST DISEASE; INTRADUCTAL PAPILLOMA; MOLECULARLY TARGETED THERAPIES; MUTATION; OBESITY AND HEALTH; ONCOGENES; SMOKING AND HEALTH; STAGING AND GRADING OF CANCER; SURGERY BENEFIT AND RISK ASSESSMENT.

breastfeeding The process of nourishing an infant with milk the mother's breasts produce. Health experts recommend breastfeeding at least for the first six months of life when possible. BREAST milk provides the ideal nutritional balance for the infant. It also conveys important antibodies to the infant, helping provide immune protection while the infant's own IMMUNE SYSTEM is develop-

ing. Breastfeeding, also called nursing, further supports a strong physical and emotional connection between mother and baby.

Though breastfeeding suppresses a woman's normal hormonal cycle to some extent, breastfeeding is not a reliable method of CONTRACEPTION (birth control). It is still possible for a nursing mother to get pregnant.

First Milk: Colostrum

The first milk the mother's breast produces after birth is colostrum, often called premilk. Colostrum is more concentrated than mature breast milk and contains primarily carbohydrate and protein with little fat. This composition is very easy for the infant to digest in the first use of the gastrointestinal system; its concentration delivers more nutrition with less volume. Colostrum also contains a higher concentration of antibodies than mature breast milk. The infant should breastfeed about every two hours in its first few days of life, both to provide sufficient nutrition and to encourage adequate milk production.

Milk Production

The hormones of PREGNANCY establish the initial environment for milk production. The stimulation of the infant's sucking induces the hormonal responses that cause the lactiferous glands of the breasts to produce milk. The lactiferous ducts store some breast milk, though the lactiferous glands actively produce milk as the infant nurses. The breasts will continue producing milk after pregnancy for as long as the baby nurses regularly.

The breast releases mature milk in two surges. The first surge, the foremilk, is thin, bluish, and contains primarily lactose (a simple carbohydrate) and proteins. The second surge, which releases after the infant has nursed for three to five minutes, is hindmilk. Hindmilk is thicker, yellowish, and contains a higher concentration of fats that are essential to supply the infant with a source of energy. The infant may nurse 10 to 30 minutes on hindmilk.

Let the Infant Take the Lead

Lactation and nutrition experts currently recommend that the mother allow the infant to nurse

completely at one breast before switching to the other, even if the infant becomes satiated before switching or before finishing the second breast. The infant generally will pull away from one breast when ready to switch. Following the infant's lead in this way, rather than breastfeeding by the clock, allows the infant to receive maximum nutritional benefit from breastfeeding. Though conventional wisdom has long held that the mother should switch the infant from one breast to the other to provide equal time at each breast under the premise that this practice would to stimulate and sustain the most ideal milk production, recent research suggests the infant may not receive balanced nutrition with such an approach. As well, sucking provides emotional comfort for the infant.

Though breastfeeding is a natural process, the process of breastfeeding does not come naturally for most women. It takes time and patience for the mother to synchronize with the baby's needs and preferences. Birthing centers have lactation specialists who can help new mothers establish effective breastfeeding. New mothers often worry the infant is not receiving enough nourishment. The most accurate measure of this is the infant's steady and appropriate weight gain and development. The breasts seldom drain completely of milk, and the infant may nurse more aggressively at some feedings than others.

Care of the Breasts

The mother's breasts, especially the nipples, are often tender during the first few weeks of breastfeeding. It is important for the infant to latch around a good portion of the areola as well as the nipple when nursing, which properly stimulates the lactiferous glands as well as eases CHAFING and soreness of the nipples. A lactation specialist can help a new mother find the nursing positions that are most effective.

Washing the breasts with warm water after breastfeeding and allowing them to air dry helps prevent irritation and chafing. A nursing bra provides extra support for the breasts, which are quite heavy and enlarged during breastfeeding. Nursing pads inserted inside the bra protect leaking milk from staining clothing. Because many substances pass from the mother's body into the

breast milk, the woman should check with her health-care provider before taking over-the-counter (OTC) medications. Certain foods appear to bother some infants, probably altering the taste or smell of the breast milk.

Expressing and Storing Breast Milk

Many women express (pump) milk from their breasts to store for feeding the baby when breastfeeding is not possible, such as after the woman returns to work. This allows other people to use a bottle to feed breast milk to the baby. Expressed breast milk will remain fresh for one week when refrigerated and for four months when frozen. Breast pumps simulate the rhythmic pressure of nursing, initiating the letdown REFLEX and releasing milk. It may take longer to express full breasts when pumping than when the baby nurses, though it is important to get as much milk as possible so milk production remains constant. The breasts adjust how much milk they produce according to the demand for milk.

See also ANTIBODY; BREAST HEALTH; MASTITIS.

breast health Measures a woman can take throughout her life to maintain the best possible health for her breasts. Because there is such wide variation around what is "normal" when it comes to breasts, health experts urge women to become familiar with the appearance and feel of their own breasts so they can easily and quickly detect changes that warrant further medical evaluation. A comprehensive approach combines lifestyle habits that support BREAST health with monthly BREAST SELF-EXAMINATION, regular breast exams from a health-care provider, and MAMMOGRAM (when age appropriate).

A woman's breasts are somewhat dynamic in that they undergo cyclic changes that follow the MENSTRUAL CYCLE. The glandular tissues respond to ESTROGENS and PROGESTERONE in the woman's BLOOD circulation. The same hormonal patterns that prepare the UTERUS for PREGNANCY also prepare the breasts to produce milk. They also cause cyclic changes in the breasts. Many women find their breasts become tender and somewhat swollen during the week before their menstrual periods—the luteal or secretory phase of the menstrual cycle when estrogen levels are especially high.

Women who have fibrocystic breasts may experience increased symptoms during this time. Knowing these cyclic patterns makes it easier to distinguish normal from unusual changes.

Lifestyle factors that influence breast health include EATING HABITS, physical exercise, and cigarette smoking. Some research studies suggest a diet high in saturated fat (animal fat) raises the risk for FIBROCYSTIC BREAST DISEASE and BREAST CANCER. The findings of other studies are inconclusive. There is increased risk for breast cancer with OBESITY, however, which may be a consequence of diet and exercise or a function of increased estrogen in the blood circulation as a result of aromatase conversion of stored estrogen in adipose (fat) cells. Numerous studies associate cigarette smoking with increased risk for fibrocystic breast disease, fibroadenoma (noncancerous breast tumor), breast cancer, and cancer overall.

See also DIET AND HEALTH; EXERCISE AND HEALTH; MASTITIS; OBESITY AND HEALTH; SMOKING AND HEALTH; SMOKING CESSATION.

breast self-examination A method a woman can use to examine her breasts for changes such as lumps and irregularities in the BREAST tissue. The primary purpose of breast self-examination (BSE) is to familiarize a woman with the normal appearance and feel of her breasts so she can detect changes that may warrant medical evaluation. Though most lumps and irregularities a woman detects through BSE are benign (noncancerous), BSE can result in early discovery of BREAST CANCER. The risk for breast cancer increases with age and is highest after MENOPAUSE.

The ideal time to perform BSE is at the end of the menstrual period when the breasts are least sensitive. BSE takes only a few minutes, following these steps:

1. Stand in front of a mirror, unclothed, with arms at the sides. Look at the breasts for any indentations, irregularities, or distortions to the shape of the breast.
2. Raise the arms and repeat the visual examination.
3. With the flat surfaces of the fingers of the left hand, gently feel the right breast starting at the nipple and moving outward in a circular pattern to cover the entire breast. Also feel into the armpit area, which contains breast tissue.
4. Gently squeeze the nipple to detect any discharge.
5. Repeat steps 3 and 4 for the left breast.
6. Lie on the back on a flat surface with the right hand behind the head. Repeat steps 3 and 4.
7. Switch to put the left hand behind head and repeat steps 3 and 4 for the left breast.

Though BSE primarily targets women, it is good preventive health for men to also become familiar with the appearance and feel of their breasts. Breast cancer is rare but can occur in men. Though lumps in the breast are easier to detect in men, men are more likely to disregard them as insignificant. A doctor should evaluate any lump that develops in a man's breast.

See also MAMMOGRAM; PREVENTIVE HEALTH CARE AND IMMUNIZATIONS; TESTICULAR SELF-EXAMINATION.



cancer of the penis A malignant (cancerous) tumor that arises from the tissues of the PENIS. Cancer of the penis is rare and usually occurs in men over age 50. Men who are uncircumcised and men who have HUMAN PAPILLOMAVIRUS (HPV) infection have increased risk for cancer of the penis. Early symptoms include a painless growth, bump, or sore at the tip of the penis. In an uncircumcised man such a growth most commonly appears beneath the foreskin, which often delays the cancer's detection. Early diagnosis and treatment allow the least invasive treatment. Surgery is the preferred treatment to remove the cancerous tumor and a safe margin of healthy tissue. Follow-up surgery to reconstruct the penis is sometimes necessary. Depending on how advanced the cancer is, the oncologist may recommend RADIATION THERAPY OR CHEMOTHERAPY in addition to surgery.

See also CANCER TREATMENT OPTIONS AND DECISIONS; [CIRCUMCISION](#); METASTASIS; PROSTATE CANCER; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; PLASTIC SURGERY; SURGERY FOR CANCER; [TESTICULAR CANCER](#).

cervical cancer A malignant (cancerous) tumor that originates in a woman's CERVIX. The cervix is a thick neck of tissue that joins the VAGINA and the UTERUS. INFECTION with the HUMAN PAPILLOMAVIRUS (HPV) accounts for nearly all cervical cancer, though only about 15 of the 100 or so strains of HPV are connected with cervical cancer and only a small percentage of women who have HPV infection with one of those strains actually develops cervical cancer.

Cervical cancer tends to follow a predictable path of development that takes many years to evolve, typically 10 years or longer. Because of

this, with early detection cervical cancer is one of the most curable forms of cancer. The path of development for cervical cancer begins with slight changes in the cells of cervical tissue, called cervical DYSPLASIA. Though not cancer, dysplasia is a circumstance of irregular cell growth. All cervical cancer begins as cervical dysplasia. Because of this, even though only a small percentage of cervical dysplasia become cancer doctors consider cervical dysplasia a broad classification of cell abnormalities that range from precancerous to cancerous.

Doctors call moderate to severe cervical dysplasia, which is precancerous, CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN). Doctors believe about two thirds of untreated cervical dysplasia progresses to cancer. The PAP TEST, a laboratory examination of cells swabbed from the cervix, can detect cervical dysplasia, CIN, and other changes in cervical tissue. A Pap test is part of a routine PELVIC EXAMINATION.

Symptoms and Diagnostic Path

Cervical cancer often shows no symptoms until it spreads outside the cervix, which is why routine Pap tests are so crucial in its detection. When symptoms are present they may include

- watery, sometimes blood-tinged discharge
- vaginal bleeding between menstrual periods or after MENOPAUSE
- vaginal bleeding during or after SEXUAL INTERCOURSE
- unusually heavy or prolonged menstrual periods
- low back discomfort
- unexplained tiredness, lack of energy, or fatigue
- URINARY URGENCY OR URINARY FREQUENCY

The diagnostic path begins with pelvic examination, Pap test, and HPV testing, including HPV DNA. COLPOSCOPY (examination of the cervix with a special lighted microscope) provides additional information about the location and extensiveness of the cancer. Cervical biopsy (laboratory examination of tissue samples taken from the cervix) provides definitive diagnosis. Diagnostic imaging procedures such as COMPUTED TOMOGRAPHY (CT)

SCAN OR MAGNETIC RESONANCE IMAGING (MRI) may show the extent to which the cancer has metastasized to locations within or distant from the pelvis. The pathologist determines the grade (degree of abnormality of the cells) and stage (extent of the tumor) from the biopsy tissue samples. STAGING AND GRADING OF CANCER is important for determining appropriate CANCER TREATMENT OPTIONS AND DECISIONS.

BASIC STAGING OF CERVICAL CANCER		
Stage	Meaning	Treatment Options
cervical intraepithelial neoplasia (CIN2/CIN3)	cells are abnormal but precancerous and confined to a localized area of the CERVIX	cryosurgery, laser surgery, loop electrosurgical procedure (LEEP), or excisional conization to remove abnormal cells frequent and regular PAP TEST and COLPOSCOPY
CIN4/stage 0/carcinoma in situ	cancer remains confined to the cells of its origin	cryosurgery, laser surgery, LEEP, or excisional conization to remove abnormal tissue frequent and regular Pap test and colposcopy
stage 1	cancer remains confined to a small, clearly defined area of the cervix stage 1A is microscopic; stage 1B is barely visible to the unaided eye	stage 1A: total HYSTERECTOMY frequent and regular Pap test and colposcopy stage 1B: modified radical HYSTERECTOMY with SENTINEL LYMPH NODE DISSECTION and adjuvant RADIATION THERAPY and/or CHEMOTHERAPY or high-dose external beam radiation combined with internal seeding
stage 2	cancer has spread to other structures within the pelvis but not to distant organs stage 2A involves the upper VAGINA; stage 2B involves parametrial tissue	high-dose external and internal radiation therapy in combination with platinum-agent chemotherapy
stage 3	cancer has spread widely within the pelvis and may involve the lower vagina and ureters stage 3A involves the lower vagina but not the pelvic wall; stage 3B involves the pelvic wall or the pelvic LYMPH nodes	combination chemotherapy palliative radiation therapy clinical trials
stage 4	cancer has spread to distant organs or recurred (come back) after treatment stage 4A involves lower abdominal organs; stage 4B involves distant organs	combination chemotherapy palliative radiation therapy clinical trials

Treatment Options and Outlook

Cervical cancer is almost always curable with minimally invasive treatment when doctors detect it as CIN or stage 1. Stage 2 and stage 3 cervical cancers require more invasive treatments and have lower potential for cure. The primary treatment of choice for most stage 1 cervical cancers is surgery to remove the tumor, the entire cervix, or, in more advanced stages, the cervix and adjacent tissues such as the upper vagina and often the uterus (total or modified radical Hysterectomy). Adjuvant (follow-up) treatment may include Chemotherapy or Radiation Therapy. High-dose radiation therapy (external beam and internal seeding) in combination with chemotherapy, is the primary treatment of choice for most stage 2 and stage 3 cervical cancers as these have usually spread beyond the scope of surgery, though surgery may be an option for stage 2 cervical cancer that remains confined to the upper vagina. The treatment of choice for stage 4 cervical cancer is combination chemotherapy with palliative radiation therapy to relieve symptoms of obstructive tumors.

CHEMOTHERAPY AGENTS TO TREAT CERVICAL CANCER

carboplatin	cisplatin
gemcitabine	paclitaxel
topotecan	vinorelbine

Risk Factors and Preventive Measures

The key risk factors for cervical cancer are HPV infection with one of the few strains of HPV linked to cervical cancer, multiple sexual partners, and cigarette smoking. The HPV vaccine prevents infection with HPV types 6, 11, 16, and 18, the strains of HPV associated with genital warts and cervical cancer. Health experts recommend HPV vaccination for girls beginning at age 12, though women to age 26 can receive the vaccine. Because HPV accounts for nearly all cervical cancer, measures to reduce exposure to HPV infection (such as condom use and mutual monogamy) are also crucial. Routine pelvic examination with Pap test can detect cervical cancer in its earliest, curable stages.

See also [BREAST CANCER](#); [CONTRACEPTION](#); [ENDOMETRIAL CANCER](#); [HIV/AIDS](#); [SEXUAL HEALTH](#); [SEXUALLY TRANSMITTED DISEASE \(STD\) PREVENTION](#); [SURGERY BENEFIT AND RISK ASSESSMENT](#).

cervical intraepithelial neoplasia (CIN) The growth of abnormal cells within the tissue of the CERVIX. Because without treatment CIN often progresses in severity and is the foundation of CERVICAL CANCER, doctors consider CIN a precancerous condition and grade it according to the extent to which it infiltrates the cervix. The four grades, or levels of severity, of CIN are

- grade 1, or CIN1, in which the abnormal cells infiltrate only the first layer of tissue; CIN1 often goes away on its own though merits careful observation until it is clear that it has done so
- grade 2, or CIN2, in which the abnormal cells penetrate to the second or third layer of tissue; standard treatment is surgical removal of the affected tissue using the loop electrosurgical excision procedure (LEEP)
- grade 3, or CIN3, in which the abnormal cells penetrate through the third layer of tissue and involve a fairly substantial area of cervical tissue; standard treatment is surgical removal of the affected tissue, usually using LEEP and sometimes using conization
- grade 4, or carcinoma in situ, in which the abnormal cells completely penetrate all epithelial layers using conization

Though CIN often follows an orderly progression from grade 2 to grade 4, culminating with cervical cancer, it does not always do so. About a third of CIN2 and CIN3 progresses to the next level and three fourths of women who have CIN4 or carcinoma in situ eventually develop cervical cancer. However, CIN1 progresses to cervical cancer in only 1 percent of women.

Symptoms and Diagnostic Path

Often a woman has no symptoms of CIN; the doctor detects the condition during routine PELVIC EXAMINATION and PAP TEST. COLPOSCOPY (examination of the cervix with a lighted surgical microscope) can sometimes confirm the diagnosis. However, excisional biopsy (removal of the abnormal area and laboratory examination of the tissue) is the definitive diagnostic procedure.

Treatment Options and Outlook

Standard treatment for CIN is removal of the abnormal cells with follow-up pelvic exam, Pap test, and other pathologic tests. The procedures for removal include

- LEEP, an office procedure in which the gynecologic surgeon inserts a wire loop through the VAGINA to the cervix and removes slices of tissue by sending a mild electrical current through the wire loop; LEEP is the standard treatment for CIN2 and some CIN3
- conization, also called excisional conization or cone biopsy, in which the gynecologic surgeon removes larger areas of tissue with instruments inserted through the vagina; the woman usually undergoes general ANESTHESIA, and the procedure is performed in an operating room

These treatments usually cure the CIN, though doctors recommend regular follow-up Pap tests, colposcopy, and other laboratory tests for up to five years after the initial treatment.

Risk Factors and Preventive Measures

The strongest risk for CIN is INFECTION with HUMAN PAPILLOMAVIRUS (HPV). CIN is more common in women who smoke and in women who have HIV/AIDS. A Pap test can detect CIN in its early, easily treatable stages. Preventive measures include safer sex methods (such as abstinence, condom use, or mutually monogamous sexual relationships) to prevent HPV infection. In 2006 the first vaccine to prevent HPV infection in women became available. The vaccine protects against infection with HPV types 6, 11, 16, and 18, the types associated with genital warts and cervical cancer. Health experts recommend HPV vaccination for girls beginning at age 12, though women to age 26 can receive the vaccine.

See also CANCER TREATMENT OPTIONS AND DECISIONS; CELL STRUCTURE AND FUNCTION; SURGERY BENEFIT AND RISK ASSESSMENT.

cervix The neck of the UTERUS, a thick cuff of muscular tissue about one inch in length that joins the VAGINA to the uterus. A narrow channel through the cervix, the cervical canal, allows menstrual material to leave and SPERM to enter the

uterus. The opening of the cervix within the uterus is the internal os; the opening of the cervix within the vagina is the external os. The cervix has the ability to thin and dilate to permit CHILD-BIRTH.

HEALTH CONDITIONS THAT MAY AFFECT THE CERVIX

CERVICAL CANCER	cervical DYSPLASIA
cervical erosion	CERVICAL INTRAEPITHELIAL
cervical polyps	NEOPLASIA (CIN)
CHLAMYDIA INFECTION	GONORRHEA
HUMAN PAPILLOMAVIRUS (HPV)	incompetent cervix during
infection	PREGNANCY
trauma	

For further discussion of the cervix within the context of the structures and functions of reproduction and sexuality, please see the overview section “[The Reproductive System](#).”

See also COLPOSCOPY; DILATION AND CURETTAGE (D&C); FALLOPIAN TUBES; GENITAL TRAUMA; HYSTERECTOMY; OVARIES; PAP TEST; PELVIC EXAMINATION.

cesarean section Surgical CHILDBIRTH. In cesarean (spelled caesarean in countries other than the United States) section, the obstetrician makes an incision through the abdominal wall and the wall of the UTERUS to extract the FETUS. Doctors in the United States perform cesarean section, also called c-section, to deliver 90 percent of breech presentations (fetus is bottom down rather than head down in the uterus) and about 25 percent of pregnancies overall. Most cesarean sections are unplanned though nonemergency, performed because of the mother’s health status, the size of the baby, or the failure of labor to progress. Emergency cesarean section may be necessary when the fetus is in distress.

Though some women feel disappointed or even dismayed to need cesarean delivery, the outcome of healthy baby and healthy mother is the overarching objective. A woman who feels rushed into surgical delivery should discuss alternatives with her obstetrician. Ideally the woman and the obstetrician have had discussions during the course of PRENATAL CARE about the circumstances under which the obstetrician may recommend cesarean section and are in agreement about them.

COMMON REASONS FOR CESAREAN SECTION

cephalopelvic disproportion	ECLAMPSIA
erratic fetal heartbeat	GENITAL HERPES outbreak
higher order multiples (triplets or more)	known serious BIRTH DEFECTS
macrosomia (very large baby)	known SPINA BIFIDA
maternal HIV/AIDS	maternal CARDIOVASCULAR DISEASE (CVD)
maternal DIABETES	nonprogressive labor
PLACENTA abruptio	placenta previa
PREECLAMPSIA	previous CESAREAN SECTION
previous uterine surgery	prolapsed UMBILICAL CORD

Most hospitals allow the woman’s partner to be present in the operating room during nonemergency cesarean delivery. The partner must change into sterile clothing (scrubs) and remain outside the sterile field, usually seated beside the woman’s head; the delivery team will provide clear and specific instruction for the partner. A draped sheet provides a screen to block the woman’s view of the OPERATION as it is taking place. Except in emergency situations when time is crucial, ANESTHESIA is nearly always epidural (injection of the anesthetic DRUG into the space around the SPINAL CORD) or spinal. These forms of anesthesia provide complete PAIN relief for the mother but do not affect the infant. General anesthesia, because the drugs enter the mother’s BLOOD circulation, affects the infant and may suppress BREATHING and HEART RATE.

Surgical Procedure

After the anesthesia takes effect, the obstetrician makes an incision through the SKIN and abdominal muscles to expose the uterus, then makes an incision through the wall of the uterus to deliver the baby. The most common incision is the low transverse (also called the bikini cut), running horizontally across the lower abdomen just above the pubic BONE about at the pubic hair line. An alternative incision for rapid delivery is the vertical incision, which extends from the umbilicus (belly button) to just above the pubic bone.

The obstetrician first delivers the baby’s head and thoroughly suctions the secretions from the NOSE, MOUTH, and upper THROAT. The pressures and forces of a vaginal delivery would squeeze these secretions from the infant as it passed through the birth canal. Removing the secretions is essential to

prepare the airways for breathing. The obstetrician then delivers the rest of the baby and clamps the umbilical cord. The pediatrician examines the baby to assess its breathing and overall health. Often the obstetrician allows the woman’s partner to cut the cord and show the baby to the mother. To this point, the cesarean section takes about 10 minutes.

The rest of the cesarean section takes about 40 minutes and consists of delivering the placenta, repairing the incision into the uterus, and repairing the incision through the abdominal muscles and the skin. The anesthesiologist may administer a sedative to help the mother relax and sleep during this part, after which she goes to the recovery unit until the epidural anesthesia wears off and sensation returns.

Risks and Complications

The risk for serious complications is very low with cesarean section. Among them are unusual bleeding, blood clots, and INFECTION in the immediate postoperative period, injury to the BLADDER or ureters, and URINARY TRACT INFECTION (UTI). There is also risk, comparable to that of vaginal birth, of injury to the infant.

The path of recovery is substantially longer for cesarean section than for vaginal birth. Most women spend three to five days in the hospital for initial recovery. The doctor will prescribe ANALGESIC MEDICATIONS to relieve pain that are safe for the woman to take while she is BREASTFEEDING. During the first two weeks at home the woman needs to take care of her incision as the doctor instructs. Full recuperation takes six to eight weeks, during which the woman needs help lifting and caring for the baby. However, walking and other physical activities are necessary and important for HEALING as well as to keep the LUNGS clear and to help prevent blood clots.

Long-term complications are rare and are most likely to occur when the cesarean section was an emergency and the obstetrician made a vertical incision. This incision creates weakness in the abdominal wall, the muscles of which have already stretched as a consequence of the pregnancy. Proper care is essential for optimal healing. The risk of incisional HERNIA is higher with the vertical incision than the transverse incision.

Outlook and Lifestyle Modifications

While the incision is healing the woman needs substantial help carrying and lifting the infant as well as with daily activities. After healing is complete the woman may and should return to full activities, including SEXUAL INTERCOURSE as she desires. Cesarean section does not affect the ability to breastfeed for as long as the woman desires or the potential for becoming pregnant again. Vaginal delivery with subsequent pregnancies (VBAC, or vaginal birth after cesarean) is possible for about two thirds of women who had transverse incisions on the uterus. Most obstetricians consider a vertical incision on the uterus too risky for VBAC because the stress of labor may cause the incisional SCAR on the uterus to rupture.

For further discussion of cesarean section, please see the overview section “[The Reproductive System](#).”

See also [APGAR SCORE](#); POSTOPERATIVE PROCEDURES; PREOPERATIVE PROCEDURES; SURGERY BENEFIT AND RISK ASSESSMENT.

childbirth The passage of the FETUS from the UTERUS to independent life outside the woman's body as PREGNANCY culminates. The physiologic processes that establish this passage are labor and delivery (vaginal birth); childbirth may also occur as a surgical procedure (CESAREAN SECTION). Labor refers to the progressively intense contractions of the uterus that dilate and efface (stretch and thin) the CERVIX, then push the fetus into and through the VAGINA (birth canal).

Though labor and delivery occur in predictable and sequential stages, their timing varies widely. Early labor may last a few to 36 hours. Active labor generally lasts 2 to 8 hours. Delivery, the passage of the baby through the birth canal, may take 15 minutes to 2 hours. A woman's first delivery typically takes longer than subsequent deliveries. Though childbirth is a natural process, in the United States most childbirth takes place in hospitals or birthing centers with medical professionals (doctors, nurses, midwives) providing care and assistance.

Stage 1: Labor

Labor is the work of the uterus and abdominal muscles to ready the woman's body for birth and

ultimately push the infant out. For more than 40 weeks the body's focus has been on maintaining the pregnancy within it. As the time for birth approaches, hormonal signals initiate the sequence of events that will make delivery possible. Researchers do not know what starts the hormonal cascade that ultimately results in childbirth, though these changes begin some time before actual labor starts.

Though the most intense experience of labor is in the hours that lead to delivery, the preparations actually begin several weeks before birth. One of the earliest signs of impending birth is the dropping of the presenting part of the fetus, usually the head, into the start of the cervix. Called engagement or lightening, this movement indicates the cervix is beginning to efface. It also signals changes that are occurring within the fetus to prepare it for life outside the womb, notably expansion of the LUNGS.

As the cervix continues to efface and begins to dilate the plug of mucus that formed in the cervical canal comes loose and slides out, which the woman may notice as a brownish discharge (sometimes called bloody show). This may occur a week or longer before birth. The characteristic experience of labor begins with sensations of tightening and relaxing in the lower abdomen, somewhat similar in experience to menstrual cramps. Many women feel these sensations in the lower back as well. The woman may feel restless and want to walk around; walking helps strengthen and coordinate contractions as they progress. Labor becomes more intense and focused when the membranes rupture, often called water breaking.

There are many ways women cope with the discomfort of labor, which intensifies as the labor progresses. Methods such as relaxation BREATHING, massage, acupuncture, and visualization often help a woman feel calm and centered. Some women become intensely active in the early stages of labor, cleaning house and otherwise “nesting.” Doctors believe this behavior harkens to primal instincts of preparedness. In early labor contractions may be 10 to 15 minutes apart and last about 30 seconds and may become less intense with certain positions or activities. As early labor progresses to active labor, contractions are about 5 minutes apart and last for 45 to 60 seconds.

In active labor contractions continue to increase in frequency and intensity, and discomfort progresses to PAIN. Many women feel the need for pain relief during active labor. Common methods include narcotic ANALGESIC MEDICATIONS and regional ANESTHESIA such as epidural block. Active labor dilates the cervix to 7 or 8 centimeters.

The final stage of labor is transition, during which contractions come in waves often without more than seconds between them. Transition consumes the woman's attention and focus; she often is not aware of activity taking place around her. Many women feel the urge to push, though should not do so because the cervix is not yet ready. Transition is usually complete within three hours. The cervix finishes dilating to a wide-open 10 centimeters, and birth is imminent.

Stage 2: Delivery of the Baby

Delivery requires much conscious effort from the woman to push with contractions. The birthing team coaches and guides the process. The urge to push may be overwhelming; going with it is usually the most efficient approach unless the doctor or midwife advises to wait. Sometimes the baby's position in the birth canal becomes awkward such that waiting a few moments allows a turn or movement that then responds better to pushing. An epidural for pain relief tends to extend delivery somewhat because the woman does not as strongly feel the urge to push.

The head emerges first, with the shoulders and then the rest of the body following. The doctor or midwife suctions any mucus and BLOOD from the baby's NOSE and MOUTH. The baby begins breathing as soon as his or her body clears the birth canal and the chest can expand. When all is well, the doctor or midwife places the baby on the mother's chest for her to hold and clamps the UMBILICAL CORD in two places. The partner, the mother, an older sibling present for the birth, or the birthing attendant may cut between the clamps to sever the cord.

Stage 3: Delivery of the Placenta

After a brief pause contractions resume to separate the PLACENTA from the endometrium and push it from the body. It takes about 10 minutes to deliver the placenta, which sometimes requires

the woman to bear down to help push it out. The uterus then continues mild contractions, which are important to restore its firmness and to stop bleeding. A member of the birthing team may massage the mother's lower abdomen to further stimulate these contractions. BREASTFEEDING the infant at this time is also helpful because the sucking at the BREAST releases OXYTOCIN, a HORMONE that continues the uterine contractions as well as releases colostrum (premilk) for the infant.

For further discussion of childbirth, please see the overview section "[The Reproductive System.](#)"

See also [POSTPARTUM DEPRESSION](#); [PRENATAL CARE](#); [VBAC](#).

chordee A congenital (present at birth) downward curvature of the PENIS. Chordee results from extra connective tissue that contracts the ventral surface of the penis, pulling the tip of the penis downward. Chordee typically occurs in conjunction with HYPOSPADIAS, a CONGENITAL ANOMALY in which the opening of the URETHRA (the meatus) is on the underside of the penis rather than at the tip. Chordee may be apparent only during ERECTION or may contract the penis significantly enough to prevent normal URINATION. Mild chordee that does not interfere with urination or SEXUAL INTERCOURSE does not require treatment. For more severe chordee, surgery to release the connective tissue and, if necessary, to correct the hypospadias relieves the curvature.

See also [CIRCUMCISION](#); [PEYRONIE'S DISEASE](#); [PHIMOSIS](#); [SURGERY BENEFIT AND RISK ASSESSMENT](#).

chorionic villi sampling (CVS) A diagnostic procedure, also called chorionic villus sampling, in which the obstetrician removes small clusters of cells from the hairlike edges of the PLACENTA, the chorionic villi, during PREGNANCY. The cells in this sample provide genetic information about the FETUS that can rule out or diagnose GENETIC DISORDERS such as CYSTIC FIBROSIS and TAY-SACHS DISEASE, NEURAL TUBE DEFECTS such as SPINA BIFIDA, or CHROMOSOMAL DISORDERS such as DOWN SYNDROME. The obstetrician can perform CVS in the first trimester, usually around the 11th week, providing information about potential health concerns early in the pregnancy to allow the woman and her partner to consider possible treatment options as well as

whether, with severe disorders or deformities, to continue the pregnancy.

To withdraw the sample of cells the obstetrician may insert a needle through the abdominal wall and into the UTERUS, similar to AMNIOCENTESIS, or may guide a very small catheter through the VAGINA and CERVIX into the uterus. The obstetrician first numbs either the site on the abdomen or the cervix with a local anesthetic, then uses ULTRASOUND to help place the needle or the catheter. After the procedure the woman may feel mild cramping or experience slight bleeding, which are the main risks associated with CVS. Rarely CVS can cause spontaneous ABORTION (loss of the pregnancy), though the risk with CVS less than the risk with amniocentesis, another prenatal diagnostic procedure, because CVS does not require penetration of the amniotic sac.

The findings available through CVS are not always as definitive as the results of amniocentesis. The advantages of CVS over amniocentesis, however, are twofold. First, the obstetrician can conduct CVS in the first trimester though cannot perform amniocentesis until well into the second trimester. Second, the risk for complications, including injury to the fetus and spontaneous abortion, is lower with CVS. It is important to discuss and thoroughly understand the reasons for either procedure.

See also ALPHA FETOPROTEIN (AFP); CONGENITAL ANOMALY; PRENATAL CARE.

circumcision The surgical removal of the foreskin (prepuce), the thin hood of SKIN that covers the end of the PENIS. The reason for circumcision may be therapeutic, religious, ceremonial, hygienic, cultural, or social. About two thirds of newborn boys in the United States are circumcised shortly after birth for nontherapeutic reasons. Nontherapeutic circumcision should take place within three weeks of birth when done in infancy. Circumcision at an older age, and particularly in adulthood, becomes a more significant surgical procedure with increased risk for complications.

Infant (Neonatal) Circumcision

For infant circumcision, the doctor applies an anesthetic cream or injects a local anesthetic to numb the penis, then applies a circumcision clamp

and cuts away the end of the foreskin. The procedure takes about 10 minutes. Some methods leave a plastic ring around the penis that seals the edge of the wound; the ring falls off when the wound heals (within 7 to 10 days). There are no sutures (stitches). Minor bleeding for a day or so after the procedure is common.

Adult Circumcision

Adult circumcision is a minor surgery OPERATION generally performed in a hospital operating room or an AMBULATORY SURGERY FACILITY; it requires regional anesthesia (anesthetic injected into the NERVE that serves the penis) and a general sedative. The circumcision operation takes about 30 minutes; typically a urologist performs the operation. Sutures remain in place for five to seven days after the operation. It is important to try to avoid erections and sexual activity for four to six weeks to allow the surgical wound to heal properly. There is often mild to moderate discomfort during HEALING; the doctor may prescribe or recommend ANALGESIC MEDICATIONS for PAIN relief.

Risks and Complications

Risks associated with circumcision include excessive bleeding, injury to the penis, too much or too little foreskin removed, and postoperative INFECTION. Infants who have a CONGENITAL ANOMALY of the penis such as HYPOSPADIAS or CHORDEE should not undergo circumcision. Health conditions for which circumcision is therapeutic include PHIMOSIS and PARAPHIMOSIS, conditions in which the foreskin does not properly retract or return to its normal position, and chronic or persistent BALANITIS (an infection of the glans that develops under the foreskin).

Medical Debate about Routine Infant Circumcision

Despite its frequency, routine infant circumcision is a matter of considerable debate among health professionals. In 1999 the American Academy of Pediatrics issued a position statement that there are no medical or health reasons for routine circumcision of newborns. Numerous studies have attempted to determine whether circumcision provides health benefits. The findings are mostly inconclusive, with the exception of a significantly increased risk in uncircumcised boys for URINARY

TRACT INFECTION (UTI) during early childhood. Uncircumcised men are more likely to acquire infections such as balanitis and perhaps SEXUALLY TRANSMITTED DISEASES (STDs) such as HUMAN PAPILLOMAVIRUS (HPV) and HIV/AIDS. Circumcision does not provide protection against such infections, however.

See also [CANCER OF THE PENIS](#); CULTURAL AND ETHNIC HEALTH CARE PERSPECTIVES; SURGERY BENEFIT AND RISK ASSESSMENT.

clitoris An organ of the female GENITALIA, located at and partially beneath the junction of the upper folds of the labia. Made of erectile tissue and nerves, the clitoris arises from the same embryonic cells as the male PENIS and, though much smaller, contains parallel structures. Two fused corpora cavernosa (spongy, tubelike channels) form the body of the clitoris, which is about an inch long. During sexual arousal the corpora cavernosa engorge with BLOOD and cause the clitoris to enlarge and become erect. At the end of the clitoris is a small bulb of highly sensitive NERVE tissue, the glans. A thin sheath, the prepuce (analogous to the male foreskin), covers the clitoral glans except during sexual stimulation when it retracts to expose the glans. The only known purpose of the clitoris is sexual stimulation, which increases vaginal lubrication and other physiologic changes to facilitate penetration during SEXUAL INTERCOURSE.

See also [ERECTION](#); [GENITAL TRAUMA](#); SEXUALITY.

colposcopy A diagnostic procedure in which the gynecologist examines a woman's external GENITALIA and the interior VAGINA using a lighted magnifying instrument called a colposcope. The gynecologist may also visualize the CERVIX though the colposcope remains outside the vagina. The colposcope allows the gynecologist to more closely examine the surface of the genital tissues when a PELVIC EXAMINATION or a PAP TEST reveals possible abnormalities. Colposcopy helps the gynecologist determine whether biopsy (removing a small sample of tissue) or another diagnostic procedure is necessary. The gynecologist performs colposcopy as an office procedure that requires no special preparation or anesthetic. Most women find colposcopy no more uncomfortable than a routine

PELVIC EXAMINATION though any associated biopsy may cause minor discomfort and slight bleeding for a day or two after the biopsy. There are no aftereffects or risks for complication with colposcopy alone.

See also [HYSTEROSCOPY](#).

conception The culmination of fertilization (union of a SPERM and an ovum) and implantation of the resulting blastocyst into the endometrium (lining of the UTERUS). Conception marks the onset of PREGNANCY.

Numerous factors, internal and external, influence conception. Internal factors include a woman's HORMONE levels and OVULATION patterns, the viability of the man's sperm, and circumstances that occlude the FALLOPIAN TUBES to keep sperm and ovum from meeting, such as scarring from PELVIC INFLAMMATORY DISEASE (PID). External factors that influence conception include cigarette smoking and birth control methods intended to block conception, such as condoms, the intrauterine device, and oral contraceptives (birth control pills).

Health conditions such as ENDOMETRIOSIS and UTERINE FIBROIDS may prevent the pregnancy from proceeding after implantation takes place, resulting in early spontaneous ABORTION (commonly called miscarriage) often before the woman realizes she has conceived.

See also [ASSISTED REPRODUCTIVE TECHNOLOGY \(ART\)](#); CONTRACEPTION; [FAMILY PLANNING](#); [FERTILITY](#); [INFERTILITY](#); [OVA](#); [ZYGOTE](#).

contraception Any of various methods, also called birth control, intended to prevent PREGNANCY. Contraception allows sexually active women and their partners to prevent as well as plan pregnancies.

The US Food and Drug Administration (FDA) approved the first oral contraceptive in 1960. Thirteen years later the US Supreme Court legalized elective ABORTION. Though they remain controversial even today, these two events were pivotal in the arena of reproductive choice and planning because they were the first methods that placed contraception in the control of women. Now, nearly all forms of contraception are for the woman's use.

COMMON METHODS OF CONTRACEPTION

Method	Male or Female	Availability	Ease of Use	Effectiveness When Used Correctly
cervical cap	female	prescription only; health-care provider must measure and fit	must insert before SEXUAL INTERCOURSE must use with spermicide must remove after specified time	85 percent when woman has not had vaginal CHILDBIRTH 70 percent when woman has had vaginal childbirth
cervical shield	female	prescription only	must insert before sexual intercourse must use with spermicide must remove after specified time	85 percent
condom	male most common; female available	over the counter (OTC)	must put on before each sexual act must withdraw from partner and remove condom for disposal while PENIS remains erect female condom may be difficult to insert	male condom: 85 to 98 percent female condom: 80 to 95 percent
continuous abstinence	both	personal commitment	challenging	100 percent
contraceptive patch	female	prescription only	woman applies once a month	99.9 percent
contraceptive ring	female	prescription only	woman inserts during MENSTRUATION, leaves in place 3 weeks, then removes	98 percent
contraceptive sponge	female	OTC	must insert before sexual intercourse must remove after specified time	65 to 90 percent
depot medroxyprogesterone acetate (DMPA) injection	female	prescription only; health-care provider must administer	received every 12 weeks	99.9 percent
diaphragm	female	prescription only; health-care provider must measure and fit	must insert before sexual intercourse must use with spermicide must remove after specified time	85 to 94 percent

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Method	Male or Female	Availability	Ease of Use	Effectiveness When Used Correctly
fertility awareness methods (FAMs)	both	personal commitment	requires diligent effort from both partners	75 to 99 percent
intrauterine device (IUD)	female	prescription only; health-care provider must insert	requires no attention once inserted can stay in the UTERUS for 5 to 12 years, depending on type	99 percent
oral contraceptives	female	prescription only	daily or weekly pill	99 percent
spermicide	female	OTC	must apply before each sexual act	70 to 85 percent
tubal ligation	female	requires surgery	requires no effort after OPERATION permanent	nearly 100 percent (1 in 300 failure rate)
vasectomy	male	requires in-office operative procedure	requires no effort after operation permanent	nearly 100 percent (1 in 500 failure rate)

Common forms of contraception include barrier methods, hormonal methods, mechanical methods, chemical methods, surgical methods, timing methods, and continuous abstinence. Some methods, such as oral contraceptives (birth control pills) and diaphragms, require a doctor's prescription. Others are invasive, such as intrauterine devices (IUDs), TUBAL LIGATION, and VASECTOMY. Still other methods of contraception are available for purchase without prescription or physician approval, sold in locations from grocery and drug-stores to dispenser machines in public bathrooms. Most public health departments freely hand out over-the-counter (OTC) methods of contraception, notably condoms.

Contraceptive effectiveness relies primarily on proper use of the method and varies widely among methods as well as within a particular method. The most reliable methods of contraception are those that are in place or effective without any effort at the time of sexual activity. Methods that have the ability to provide nearly 100 percent prevention of pregnancy may actually

result in much lower prevention when not used properly. Only about 40 percent of women take oral contraceptives precisely as the label instructions direct, for example, raising the risk for unintended pregnancy.

Many people combine methods to optimize protection from pregnancy, for example using barrier contraception (condom or diaphragm) with chemical methods (spermicides). Only condoms (male or female) also provide protection against SEXUALLY TRANSMITTED DISEASES (STDs). A woman who takes oral contraceptives to prevent pregnancy but has more than one sexual partner also needs the protection of a condom. Partners also should wear condoms for sexual activity during outbreaks of GENITAL HERPES and if they are HIV positive or have HUMAN PAPILLOMAVIRUS (HPV) or HEPATITIS B or C.

Emergency contraception is available through pharmacies in the United States without a doctor's prescription. Emergency contraception, also called the "morning after pill," is a high DOSE of an oral contraceptive. The hormones in the medication

alter the environment within the UTERUS such that a fertilized ovum (egg) cannot implant. The woman must take emergency contraception no later than 72 hours after unprotected SEXUAL INTERCOURSE.

See also CONCEPTION; FAMILY PLANNING; FERTILITY; INFERTILITY; OVA; SEXUAL HEALTH; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; SPERM.

cryptorchidism Undescended testicle. The TESTICLES form within the abdominal cavity early in fetal development and normally descend through the inguinal canal at the floor of the pelvis into the SCROTUM during the third trimester of PREGNANCY. In some boys the testicle may spontaneously descend during the first year of life; after one year of age, however, this is unlikely. Numerous factors contribute to cryptorchidism, key among them being genetic and hormonal influences.

Treatment to bring the testicle outside the body is essential to preserve FERTILITY and because a testicle retained within the abdominal cavity has a high risk for TESTICULAR CANCER.

Treatment options are hormonal therapy, in which GONADOTROPIN-RELEASING HORMONE (GNRH) administration may stimulate the testicle to descend on its own, and surgery (ORCHIOPEXY) to shift the testicle from its abdominal position into the scrotum. Orchiopexy is the more common therapeutic route. Surgery sometimes involves procedures to repair related structures such as the arteries and veins that supply the testicle and the VAS DEFERENS, the tubular structure that transports SPERM from the testicle. Bilateral cryptorchism, in which both testicles are undescended, often results in sterility (permanent inability to father a child) because normal body temperature destroys the ability of the testicle to produce sperm.

Even after treatment the risk for testicular cancer remains higher than normal; boys and men who have had cryptorchidism should perform monthly TESTICULAR SELF-EXAMINATION. Most men who had successful treatment for cryptorchidism early in childhood have full fertility. Cryptorchidism does not affect sexual function.

See also FERTILITY; HYPOGONADISM; HYPOSPADIAS; SURGERY BENEFIT AND RISK ASSESSMENT.

D

dilation and curettage (D&C) A surgical procedure, also called dilatation and curettage, in which the gynecologist widens the opening of the CERVIX enough to allow passage into the UTERUS of a narrow scraping instrument called a curette. The gynecologist uses the curette to gently scrape the inside wall of the uterus, removing accumulated BLOOD and tissue that may be causing DYSFUNCTIONAL UTERINE BLEEDING (DUB) or that remains after a spontaneous ABORTION (miscarriage) or an induced abortion using abortifacients (drugs that terminate PREGNANCY).

The doctor performs a D&C in a hospital operating room or AMBULATORY SURGICAL FACILITY with the woman under general ANESTHESIA. The procedure itself takes about 15 minutes; most women are able to go home a few hours after, when they have completely emerged from the effects of the anesthesia. Discomfort similar to moderate menstrual cramps and mild bleeding may occur for up to two weeks after the D&C. Uncommon complications include unusual bleeding during or after the procedure, postoperative INFECTION, and uterine perforation, in which the curette penetrates the wall of the uterus (a small wound that typically heals without intervention). Most women are able to return to normal activities (except SEXUAL INTERCOURSE) within a few days though may feel discomfort for up to a week.

Before undergoing a D&C, a woman should confirm with her gynecologist that the benefits of the procedure outweigh the discomfort and potential complications compared to noninvasive procedures such as ULTRASOUND for diagnostic purposes or medications to treat DUB. Minimally invasive procedures such as endometrial sampling (in which the gynecologist inserts a very thin catheter through the cervix, without dilation, and into the

uterus to withdraw a small sample of tissue from the uterine wall) and HYSTEROSCOPY often can provide the same diagnostic information as would D&C but with less risk and discomfort for the woman.

See also SURGERY BENEFIT AND RISK ASSESSMENT.

dysfunctional uterine bleeding (DUB) Bleeding from the UTERUS through the VAGINA that occurs outside the hormonal bleeding normally associated with the MENSTRUAL CYCLE. Doctors believe DUB results from an imbalance between ESTROGENS and PROGESTERONE, the hormones that regulate the menstrual cycle, which allows the endometrium (lining of the uterus) to grow unchecked. The excess tissue dies and sloughs away, producing clotty bleeding.

Vaginal bleeding that saturates more than eight pads in 24 hours for longer than two days may signal a health concern other than DUB and requires prompt medical evaluation.

Symptoms and Diagnostic Path

Because there are numerous causes for abnormal vaginal bleeding, DUB is a diagnosis of exclusion: The doctor concludes the situation is one of DUB after ruling out other possible causes for the bleeding. The essential symptom of DUB is excessive vaginal bleeding. Though the bleeding often has the characteristics of a heavy menstrual period, it may not follow the timing of the woman's menstrual cycle. Some women experience DUB as episodes of bleeding that occur between menstrual periods and for other women the bleeding may be fairly constant or occur with no predictable pattern. Further symptoms of DUB

may include HOT FLASHES and mood swings. Cramping and PAIN are uncommon; these symptoms suggest a diagnosis other than DUB.

Because doctors consider DUB as a diagnosis of exclusion—that is, a diagnosis the doctor reaches after ruling out other possible causes for the bleeding—the diagnostic path may include tests for SEXUALLY TRANSMITTED DISEASES (STDs), BLOOD test to check for PREGNANCY, and other blood tests to measure estrogen, progesterone, and LUTEINIZING HORMONE (LH). A key factor in establishing the diagnosis of DUB is the absence of OVULATION, which characterizes most DUB. The doctor may also check other HORMONE blood levels such as thyroid hormones.

Treatment Options and Outlook

For most women the first course of treatment for DUB is HORMONE THERAPY to restore the body's natural estrogen–progesterone balance. For women of childbearing age this might mean oral contraceptives (birth control pills); for women near MENOPAUSE this might mean a hormone medication such as conjugated estrogens with progesterone or progesterone supplementation. The general therapeutic approach is to take hormone therapy until the menstrual cycle returns to normal, typically three to six months. Nonhormonal medications that may relieve mild DUB include NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs). Because long-term excessive bleeding commonly results in iron-deficiency ANEMIA, the doctor may also prescribe an iron supplement.

When the medication path is not sufficient, the gynecologist may choose to perform endometrial ablation, in which the gynecologist uses electrocautery, hot balloon, or surgical laser to burn away the endometrial lining and the thin layer of uterine tissue beneath it. This restores the inside of the uterus to its base level so it can resume its natural cycle of thickening and sloughing. Other surgical options include DILATION AND CURETTAGE (D&C), to gently scrap away the endometrial lining, and HYSTERECTOMY (removal of the uterus). Though DUB is one of the most common reasons for hysterectomy, hysterectomy is generally the treatment of final choice for DUB, the treatment gynecologists turn to when other treatment options are not practical or are not successful.

Because hysterectomy is a major surgery with numerous potential risks and permanently ends a woman's ability to become pregnant, it is an option that requires careful consideration.

Risk Factors and Preventive Measures

DUB occurs most often during the first and last years of the menstrual cycle. Progesterone-only methods of CONTRACEPTION may also precipitate DUB. However, there are no known measures for preventing DUB.

See also AMENORRHEA; DYSMENORRHEA; ECTOPIC PREGNANCY; ENDOMETRIAL HYPERPLASIA; HYPERTHYROIDISM; HYPOTHYROIDISM; MENSTRUATION; POLYCYSTIC OVARY DISEASE (PCOD).

dysmenorrhea Cramping, PAIN, abdominal bloating, and other discomforts associated with MENSTRUATION. Primary dysmenorrhea occurs without underlying health conditions that cause such symptoms and generally begins within two or three years of MENARCHE (the onset of menstruation). Secondary dysmenorrhea occurs because of underlying health conditions such as ENDOMETRIOSIS or UTERINE FIBROIDS and typically begins later in a woman's life as these conditions develop. Congenital anomalies that affect the way menstrual material flows from the body may also cause secondary dysmenorrhea that is present from menarche.

Doctors believe primary dysmenorrhea, which is the more common form of dysmenorrhea, results from the combination of hormonal actions that reduce BLOOD flow to the endometrium (lining of the UTERUS that thickens in the first half of the MENSTRUAL CYCLE to prepare the uterus for possible PREGNANCY) and initiate menstruation. As the body's balance of estrogen and progesterone shifts, the uterus releases PROSTAGLANDINS and vasopressin. These hormones cause the smooth MUSCLE tissue of the uterus to contract, helping expel the sloughed endometrial tissue that forms the menstrual discharge. Prostaglandins also play a key role in INFLAMMATION and sensitize NERVE endings to pain signals.

Symptoms and Diagnostic Path

Dysmenorrhea presents a characteristic spectrum of symptoms that occur in varying degrees among

different women though are usually consistent from period to period in an individual woman. These symptoms may include

- crampy pain in the lower abdomen, often extending into the lower back and sometimes occurring in a combination of steady cramps with intermittent spasms or outright pain
- sensation of heaviness in the lower abdomen
- bloating (fluid retention)
- HEADACHE
- NAUSEA and VOMITING
- bowel disturbances (CONSTIPATION OR DIARRHEA)
- fatigue

Symptoms often vary in severity over the course of the menstrual period, typically being more severe during the first two to three days of menstrual bleeding. About 10 percent of women who have dysmenorrhea have symptoms severe enough to prevent their participation in regular daily activities. The diagnostic path begins with a medical examination that includes a comprehensive health history (including history of sexual activity), PELVIC EXAMINATION, PAP TEST, and laboratory tests for SEXUALLY TRANSMITTED DISEASES (STDs). Any abnormal findings suggest secondary dysmenorrhea and require additional assessment and appropriate diagnostic procedures. Normal findings establish a presumed diagnosis of primary dysmenorrhea.

Treatment Options and Outlook

Medications are the first choice of treatment for primary dysmenorrhea. Those that provide the greatest level of relief are NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), which block the release of prostaglandins, and oral contraceptives (birth control pills), which regulate the estrogen–progesterone balance as well as reduce prostaglandin release. Some women obtain adequate relief from over-the-counter NSAIDs; other women require stronger prescription NSAIDs. For severe dysmenorrhea that does not improve with

these treatments, the gynecologist may recommend extended cycle oral contraceptives, a therapy that reduces the frequency of menstrual periods to every three months, or HORMONE THERAPY to suppress menstruation up to 12 months. Lifestyle and complementary methods for relief of symptoms include ACUPUNCTURE, thiamine supplementation, herbal therapies, dietary changes to decrease inflammation, heat to the lower abdomen or back, progesterone cream, and daily physical exercise. Treatment for secondary dysmenorrhea targets the underlying condition as well as symptom relief.

MEDICATIONS TO TREAT DYSMENORRHEA

diclofenac	ethinyl estradiol and
ethinyl estradiol and	norethindrone
norgestimate	ibuprofen
ketoprofen	meclofenamate
mefenamic acid	naproxen

Risk Factors and Preventive Measures

Menstrual cramps and associated discomforts are very common among menstruating women. Women who have a heavy menstrual flow, who have not carried a pregnancy to term, or who smoke cigarettes are more likely to have dysmenorrhea. Physical inactivity, OBESITY, and chronic PELVIC INFLAMMATORY DISEASE (PID) may also influence dysmenorrhea. Health conditions that may exacerbate dysmenorrhea include DYSFUNCTIONAL UTERINE BLEEDING (DUB), endometriosis, and uterine fibroids. Because dysmenorrhea occurs only among menstruating women, the end of menstruation brings the end of dysmenorrhea. Circumstances that end menstruation include MENOPAUSE (the natural cessation of the menstrual cycle that occurs with aging), HYSTERECTOMY (surgical removal of the uterus), and some treatments for cancer such as CHEMOTHERAPY OR RADIATION THERAPY to the abdomen.

See also AMENORRHEA; CONTRACEPTION; EXERCISE AND HEALTH; HYPERTHYROIDISM; HYPOTHYROIDISM; PRE-MENSTRUAL SYNDROME (PMS); SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; SMOKING AND HEALTH.

eclampsia A potentially life-threatening complication of PREGNANCY in which the woman experiences tonic-clonic seizures, extreme HYPERTENSION (high BLOOD PRESSURE), and periods of unconsciousness or COMA. Eclampsia threatens the well-being of the FETUS because it so dramatically affects the mother's health that prompt delivery is usually necessary, risking preterm birth when eclampsia occurs before 37 weeks gestation.

Routine PRENATAL CARE, which allows early detection of problems such as hypertension in the pregnancy, and aggressive treatment for PREECLAMPSIA, which is often though not always the precipitating condition, make eclampsia relatively uncommon in the United States. When it does occur, eclampsia usually develops between the 20th week of pregnancy and the first week after CHILDBIRTH (though sometimes occurs up to several weeks later).

Doctors do not know what causes eclampsia or what causes some women who have preeclampsia (sometimes called toxemia of pregnancy or gestational hypertension) to progress to eclampsia and others not. The treatment of choice for eclampsia is intravenous magnesium sulfate to stop the seizures with delivery of the baby as rapidly as possible. When eclampsia occurs before fetal viability (generally 24 weeks), doctors may attempt to control the hypertension and seizures in the mother to allow the fetus to further mature. However, the best outcomes for mother and baby occur with the earliest intervention possible. There are no known measures to prevent eclampsia.

See also [GESTATIONAL DIABETES](#); SEIZURE DISORDERS.

ectopic pregnancy A life-threatening circumstance in which a fertilized ovum (ZYGOTE) implants

in a location outside the UTERUS, usually in one of the FALLOPIAN TUBES though sometimes elsewhere in the abdominal cavity. A woman's body cannot support such a PREGNANCY; if an ectopic pregnancy continues beyond the very early stages of development it will cause the structure supporting (such as the fallopian tube) it to rupture. The resulting hemorrhage (uncontrolled bleeding) becomes life-threatening without treatment.

Symptoms and Diagnostic Path

Early symptoms of ectopic pregnancy typically occur before the woman realizes she may be pregnant and mimic those of the onset of MENSTRUATION. They may include

- cramping in the lower abdomen
- aching or PAIN in the lower back
- NAUSEA
- slight vaginal bleeding (spotting)

Many women do not experience early symptoms, however. The symptoms of ectopic pregnancy rapidly worsen, often over a period of hours, progressing to sharp pain in the lower abdomen and often shock and loss of CONSCIOUSNESS. Bleeding is usually internal, into the abdominal cavity, and consequently not apparent. The diagnostic path typically includes PELVIC EXAMINATION, BLOOD test for pregnancy, and abdominal ULTRASOUND. The ultrasound can detect abnormal tissues and bleeding.

Emergency medical care is essential for symptoms of ectopic pregnancy. Ectopic pregnancy cannot survive and is life-threatening for the woman.

Treatment Options and Outlook

Abortifacient medications (drugs that cause ABORTION, or loss of a pregnancy) such as methotrexate may terminate an ectopic pregnancy detected very early, avoiding the need for surgery and minimizing the risk for damage to the fallopian tubes and other structures. Such medications work by stopping cell division, affecting rapidly dividing cells such as those of the zygote. These medications were first developed, and are still used, to treat cancer, in which cells also rapidly divide.

Ectopic pregnancy that becomes at all advanced requires surgery that terminates the pregnancy and removes the tissues that have developed to support it. There may be damage to the structure where the pregnancy implanted, such as the fallopian tube or less commonly the CERVIX or ovary, that requires surgical repair. With prompt treatment most women recover fully from ectopic pregnancy though the experience of an ectopic pregnancy is often emotionally traumatic because the pregnancy cannot survive. Damage to or loss of the involved fallopian tube or ovary, if it occurs, may subsequently impair FERTILITY.

Risk Factors and Preventive Measures

Ectopic pregnancy occurs when there is a mechanical or hormonal impediment that prevents or slows the zygote's movement through the fallopian tube to the uterus after fertilization as is the normal process in establishing pregnancy. Risk factors for ectopic pregnancy include

- PELVIC INFLAMMATORY DISEASE (PID), which often results in scarring and blockage of the fallopian tubes
- congenital abnormalities of the fallopian tubes
- progesterone-only contraceptives, which work by impeding the implantation process
- TUBAL LIGATION in which the fallopian tube partially reopens and allows SPERM to escape into the abdominal cavity, or surgical reversal of tubal ligation to restore fertility
- use of an intrauterine device (IUD) for contraception
- ENDOMETRIOSIS
- abdominal adhesions (SCAR tissue), resulting from abdominal surgery such as APPENDECTOMY,

that pull the fallopian tubes out of their normal positions

- previous ectopic pregnancy

Though there are no measures to prevent ectopic pregnancy, prompt medical attention to early symptoms of ectopic pregnancy allows treatment before life-threatening complications arise. Early treatment also helps preserve fertility.

See also CHEMOTHERAPY; CONTRACEPTION; OVA.

ejaculation The forceful contractions that expel SEMEN from the erect PENIS during the male ORGASM. Though ejaculation occurs as a result of sexual stimulation, the muscular contractions that produce ejaculation are not within voluntary control. Ejaculation moves semen (SPERM and seminal fluid) from the seminal vesicles, VAS DEFERENS, and PROSTATE GLAND into the URETHRA, and then ejects it from the urethra. In a man who has had a VASECTOMY, the semen does not contain sperm. A tiny valve at the urethral entrance to the BLADDER closes across the bladder opening, directing the flow of semen through the urethra to the outside of the penis. In a man who has had a PROSTATECTOMY (surgery to remove the prostate gland), ejaculation is retrograde (the semen enters the bladder instead of exiting through the urethra) because the OPERATION also involves removal of this valve.

For further discussion of ejaculation within the context of the structures and functions of reproduction and sexuality, please see the overview section "[The Reproductive System](#)."

See also RETROGRADE EJACULATION.

embryo The stage of prebirth development from the 15th day after CONCEPTION to 8 weeks of gestational age. The embryo arises from the three germ layers of the ZYGOTE:

- The ectoderm is the outermost layer. It is the foundation for the SKIN and mucous membranes, the TEETH, and the structures of the nervous system.
- The mesoderm is the middle layer. It is the foundation for the organs and structures of the musculoskeletal, cardiovascular, pulmonary,

gastrointestinal, urinary, and reproductive systems.

- The endoderm is the innermost layer. It is the foundation for the tissues that line the inside of the gastrointestinal, urinary, pulmonary, and reproductive organs and structures.

These layers differentiate into their respective structures and organs during the embryonic stage. When this differentiation is complete, the developing life becomes a FETUS.

For further discussion of the embryo within the context of the structures and functions of reproduction and sexuality, please see the overview section “[The Reproductive System](#).”

See also [PREGNANCY](#).

endometrial cancer A malignant (cancerous) tumor, sometimes called uterine cancer, that arises from the tissues of the endometrium, the lining of the UTERUS. Often endometrial cancer is HORMONE driven, which means it requires ESTROGENS to grow. Doctors in the United States diagnose endometrial cancer in about 40,000 women each year; it is the fourth most common cancer among women. With early detection and treatment, endometrial cancer is highly treatable. Endometrial cancer tends to develop slowly, typically over years, and most commonly occurs in women over age 60.

Endometrial cancer develops when the cells that form the endometrium become disordered, often as a consequence of chronic ENDOMETRIAL

BASIC STAGING OF ENDOMETRIAL CANCER

Stage	Meaning	Treatment Options
stage 0/carcinoma in situ	cancer remains confined to the cells of its origin	total HYSTERECTOMY with optional bilateral salpingo-oophorectomy
stage 1	cancer remains confined to the body of the UTERUS	total hysterectomy with bilateral salpingo-oophorectomy and SENTINEL LYMPH NODE DISSECTION adjuvant RADIATION THERAPY
stage 2	cancer involves the uterus and the CERVIX	preoperative radiation therapy total hysterectomy with bilateral salpingo-oophorectomy and sentinel lymph node dissection
stage 3	cancer has spread beyond the uterus though remains confined to the pelvic area cancer may involve the VAGINA and LYMPH nodes adjacent to the uterus	preoperative radiation therapy radical hysterectomy adjuvant HORMONAL THERAPY
stage 4	cancer has spread to other organs in the abdomen such as the RECTUM OR BLADDER cancer has spread to distant sites	radiation therapy hormonal therapy clinical trials
stage 4 recurrent	cancer has returned after treatment	radiation therapy hormonal therapy clinical trials four to six cycles of two-drug (doxorubicin and cisplatin) or three-drug (doxorubicin, cisplatin, and paclitaxel) combination CHEMOTHERAPY IMMUNOTHERAPY

HYPERPLASIA (overgrowth of the endometrium). Endometrial hyperplasia occurs when there is an imbalance between estrogens and **PROGESTERONE** in the woman's **BLOOD** circulation. Researchers do not know what sets the stage for this imbalance. Elevated estrogens cause the endometrium to thicken and engorge with blood, and diminished progesterone fails to initiate adequate sloughing of the endometrial tissue (such as during **MENSTRUATION**). The tissue continues to accumulate, and over time its cells become abnormal.

Symptoms and Diagnostic Path

Because endometrial cancer usually develops later in life, its symptoms sometimes blend with those of **MENOPAUSE**. Because of this a doctor should evaluate symptoms that persist, even when the symptoms do not seem especially serious. Early symptoms of endometrial cancer include

- unusually long or severe menstrual periods
- spotting or bleeding between menstrual periods
- watery, blood-tinged vaginal discharge
- **PAIN** during **SEXUAL INTERCOURSE**
- pelvic or lower abdominal pain

The diagnostic path includes a comprehensive medical examination with **PELVIC EXAMINATION**, during which the doctor often can palpate (feel) a growth within the uterus or detect abnormalities in the uterus's size or shape. Diagnostic imaging procedures such as **COMPUTED TOMOGRAPHY (CT) SCAN** or **ULTRASOUND** may provide further information. However, only endometrial biopsy can provide a certain diagnosis. The doctor may obtain a tissue sample for biopsy by inserting a narrow catheter through the **VAGINA** and **CERVIX** into the uterus and aspirating (suctioning) cells from the endometrium. **HYSTEROSCOPY** or the surgical **OPERATION DILATION AND CURETTAGE (D&C)** may also provide endometrial cells for pathology analysis.

When confirming the diagnosis, the pathologist assigns a grade and stage to the cancer that characterize its aggressiveness and the extent to which it has grown or metastasized (spread to other locations in the body). Additional pathology tests determine whether the cancer cells have estrogen receptors (are estrogen positive). **CANCER STAGING**

AND **GRADING** and estrogen reception provide guidance for **CANCER TREATMENT OPTIONS AND DECISIONS**.

Treatment Options and Outlook

Total **HYSTERECTOMY**, a surgical operation to remove the uterus and cervix, is nearly always the first treatment of choice for stage 0, 1, and 2 endometrial cancers. Women who have stage 1 or stage 2 endometrial cancer subsequently undergo adjuvant (follow-up) treatment such as **HORMONE THERAPY** or **RADIATION THERAPY**. Very early endometrial cancer (stage 0, also called carcinoma in situ, and stage 1) is nearly always curable.

For stage 3 and 4 endometrial cancer, the first treatment of choice is radiation therapy to shrink the cancer, with follow-up surgery and hormonal therapy (stage 3) or hormonal therapy alone. Surgery may be total hysterectomy with salpingo-oophorectomy (removal of the uterus, cervix, **FALLOPIAN TUBES**, and **OVARIES**) or radical hysterectomy (removal of all the organs of reproduction, the fatty layer covering them called the omentum, and nearby **LYMPH** nodes). Radiation therapy may be external beam (targeted at the pelvis from a machine outside the body) or brachytherapy (implanted radioactive pellets). Though other treatment options are more effective for stage 0, 1, and 2 endometrial cancers, combination **CHEMOTHERAPY** becomes a treatment option for metastasized endometrial cancer (stage 3 and stage 4).

Most endometrial cancers are hormone sensitive. Hormonal therapy, such as progestins or estrogen antagonists, effectively shrinks cancer tumors in women by depriving their cells of the hormones they need to thrive. Progestin causes endometrial atrophy (shrinkage of the endometrium) and is an option for younger women with stage 0 or stage 1 endometrial cancer who wish to preserve their **FERTILITY**. Among the estrogen antagonists currently available are aromatase inhibitors and tamoxifen; these therapies require the cessation of ovarian function. Most women who have stage 2 and more advanced endometrial cancer undergo oophorectomy (surgical removal of the ovaries). Aromatase inhibitors block the conversion of **TESTOSTERONE** to estrogen in adipose (fat) cells throughout the body, the primary means of estrogen production in a woman's body after **MENOPAUSE**.

Risk Factors and Preventive Measures

Endometrial cancer is most common in women over age 60. Unopposed estrogen therapy (estrogen without progestin, except in women who have had hysterectomies) and long-term tamoxifen use are additional risk factors. OBESITY, INSULIN RESISTANCE, and type 2 DIABETES also increase the risk for endometrial cancer because these conditions result in higher levels of estrogens in the blood circulation. Endometrial cancer follows a predictable path of evolution from endometrial HYPERPLASIA to full-blown cancer, a path that generally takes years or even decades to manifest. This characteristic makes endometrial cancer fairly easy to detect in women who have regular routine medical examinations with pelvic examination.

See also [BREAST CANCER](#); [CERVICAL CANCER](#); [HORMONE-DRIVEN CANCERS](#); [METASTASIS](#); [OVARIAN CANCER](#); [PAP TEST](#); [PREVENTIVE HEALTH CARE AND IMMUNIZATION](#).

endometrial hyperplasia An overgrowth of the endometrium, the tissue that lines the UTERUS. The thickened endometrium fails to slough during MENSTRUATION, thus continuing to accumulate. Often menstruation is minimal or intermittent. Endometrial HYPERPLASIA in which cell DNA remains normal nearly always remains benign (does not become cancerous). Endometrial hyperplasia that consists of both abnormal cells and abnormal cell organization (architecture), though itself benign, is precancerous.

There are four types of endometrial hyperplasia:

- Simple endometrial hyperplasia (also called cystic glandular or mild hyperplasia) is the earliest stage of endometrial hyperplasia. There is excessive growth of the cells of the endometrium in confined locations though the cells and their architecture (structure and arrangement) are normal. The risk for progression to endometrial cancer is minimal; simple endometrial hyperplasia often resolves (goes away) without treatment.
- Complex endometrial hyperplasia features excessive growth of normal cells with irregular architecture, presenting a somewhat higher, though still relatively low, risk for developing into endometrial cancer without treatment. For

most women, doctors recommend treatment with progestin, a synthetic form of PROGESTERONE, to halt the actions of estrogen and cause the endometrium to wither and slough. The endometrium generally returns to normal within two or three MENSTRUAL CYCLES.

- Simple endometrial hyperplasia with atypia is a moderate stage of endometrial hyperplasia in which patches of endometrial cells are not only replicating more frequently than normal but have also become abnormal in their DNA (called nuclear atypia). However, the cellular architecture still follows the normal pattern for endometrial tissue. Untreated simple endometrial hyperplasia with atypia progresses to endometrial cancer in about 10 percent of women. Treatment with progestin often resolves the hyperplasia.
- Complex endometrial hyperplasia with atypia is the most serious stage of endometrial hyperplasia. The endometrial cells have abnormal DNA, instructing them to replicate in unstructured and dysfunctional ways. As well, the endometrial tissue that contains the atypical cells is disorganized and erratic. Without treatment, this stage of endometrial hyperplasia progresses to endometrial cancer in a third or more of women. Treatment with progestin usually, though not always, resolves the hyperplasia.

Symptoms and Diagnostic Path

Symptoms of endometrial hyperplasia may include bleeding between menstrual periods, anovulatory periods (menstrual cycles without OVULATION), heavy or prolonged menstrual periods, and PAIN during SEXUAL INTERCOURSE. Some women may experience AMENORRHEA (absence of menstrual periods). Endometrial biopsy, as an independent procedure or after DILATATION AND CURETTAGE (D&C), confirms the diagnosis. Imaging procedures are not usually helpful as they cannot conclusively distinguish between noncancerous and cancerous tumors in the uterus.

Treatment Options and Outlook

In addition to progestin therapy, other treatment options include the surgical operations D&C and HYSTERECTOMY. In D&C the surgeon gently scrapes

away the overgrown endometrium; in hysterectomy the surgeon removes the uterus. In most situations, hysterectomy is appropriate only when complex endometrial hyperplasia with atypia recurs after other treatments or when the risk for endometrial cancer is high for other reasons, though women who are past menopause and have persistent symptoms may opt for hysterectomy to permanently end the hyperplasia.

Risk Factors and Preventive Measures

Any circumstance that increases the presence of estrogen in the BLOOD circulation underlies the development of endometrial hyperplasia. The risk for endometrial hyperplasia is highest in women who have anovulatory periods (menstrual cycles without ovulation), who take unopposed estrogen therapy (estrogen alone), or who take long-term tamoxifen to treat BREAST CANCER. Other factors that increase estrogen within the body are OBESITY, INSULIN RESISTANCE, and type 2 DIABETES. Nutritional EATING HABITS that emphasize foods low in fats, especially saturated fats, and daily physical exercise are the key lifestyle measures that reduce the risk for endometrial hyperplasia.

See also CANCER RISK FACTORS; CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN); CERVIX; DYSPLASIA; DYSFUNCTIONAL UTERINE BLEEDING (DUB); SURGERY BENEFIT AND RISK ASSESSMENT.

endometriosis A condition in which endometrial tissue (the tissue that forms the lining of the UTERUS) grows abnormally in areas outside the uterus. The most common sites are the OVARIES, FALLOPIAN TUBES, peritoneal (abdominal) cavity, gastrointestinal tract (particularly the COLON), and BLADDER, though endometrial tissue may appear in other locations throughout the body. Endometrial growths, also called implants or tumors, respond to the body's changing hormonal environment through the MENSTRUAL CYCLE in the same ways as endometrial tissue within the uterus: They engorge with BLOOD, atrophy, and slough (bleed). Because there is no pathway for bleeding from these distant endometrial implants to leave the body, the blood accumulates in the surrounding tissues. INFLAMMATION develops as part of the IMMUNE RESPONSE, initiating a HEALING process that results in the formation of SCAR tissue.

The growth of endometrial tissue in the fallopian tubes or ovaries blocks the ability of these structures to properly function, a primary consequence of which is impaired FERTILITY. Endometriosis also appears to instigate an abnormal immune response in which phagocytic cells (cells that engulf and consume cellular debris), primarily macrophages, target and kill SPERM and OVA (eggs). About 40 percent of women who seek treatment for INFERTILITY have endometriosis. Endometriosis affects more than five million women in the United States.

Researchers do not know what causes endometriosis or how endometrial tissue arises in sites other than the uterus. Many women who have endometriosis often also have AUTOIMMUNE DISORDERS such as atopic DERMATITIS, ASTHMA, and allergies, giving rise to the suspicion of a dysfunction within the immune system. Some researchers believe endometrial cells escape from the uterus via the fallopian tubes, then migrate through the LYMPH or blood circulation to implant and grow in other locations. Endometriosis tends to progressively worsen over time because the endometrial implants grow under the influence of ESTROGENS, though this growth usually abates with MENOPAUSE. For most women menopause, natural or induced, ends endometriosis.

Symptoms and Diagnostic Path

The primary symptoms of endometriosis are PAIN and infertility. Pain is typically cyclic, following the pattern of the menstrual cycle, and may be moderate to debilitating, especially during MENSTRUATION. Distant endometrial implants also cause pain as they swell and then bleed. The diagnostic path includes comprehensive medical examination with pelvic examination and often pelvic ULTRASOUND. Exploratory laparoscopy provides the definitive diagnosis, allowing the gynecologist to directly visualize the endometrial implants. Diagnostic imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) often can detect distant endometrial implants.

Treatment Options and Outlook

At present there is no cure for endometriosis, though various treatment approaches, medical

and surgical, can control symptoms and improve fertility. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs), which block the inflammatory response as well as relieve pain, are often adequate to treat mild symptoms in women who wish to become pregnant. HORMONE THERAPY is highly effective to treat moderate to significant symptoms in women who do not desire to become pregnant. Common hormone therapies include

- estrogen and progestin in combination, such as oral contraceptives (birth control pills)
- progestin alone, such as in progestin oral contraceptives or DepoProvera injections
- danazol, an androgen analog (synthetic, weak male HORMONE) that suppresses the menstrual cycle
- GONADOTROPIN-RELEASING HORMONE (GNRH) antagonists such as leuprolide, which shut down the ovaries to prevent them from producing estrogen

Laparoscopic surgery to remove endometrial implants from pelvic structures and the peritoneal cavity may be the only treatment that effectively mitigates symptoms in women who have severe, disabling endometriosis. Therapeutic laparoscopy for endometriosis can provide long-term relief. However, it does not remove distant endometrial implants, which often continue to produce symptoms. As well, endometrial implants will regrow if a few endometrial cells remain.

Risk Factors and Preventive Measures

Factors that increase a woman's risk for endometriosis are unclear. Because endometriosis tends to run in families, researchers believe it may be the result of GENETIC PREDISPOSITION in combination with other, undetermined factors. However, any woman who menstruates can develop endometriosis. There are no measures to prevent endometriosis.

See also ANALGESIC MEDICATIONS; [ENDOSCOPY](#); MACROPHAGE; MONONUCLEAR PHAGOCYTE SYSTEM; PHAGOCYTOSIS; SURGERY BENEFIT AND RISK ASSESSMENT; [UTERINE FIBROIDS](#).

epididymitis INFLAMMATION of the EPIDIDYMIS, nearly always due to INFECTION. The epididymis is a

tightly coiled tubule that begins at the base of the testicle and ends at the VAS DEFERENS. The epididymis incubates newly formed SPERM, bringing them to maturation as they migrate through its coils on their journey to the vas deferens. *ESCHERICHIA COLI* INFECTION, CHLAMYDIA, and GONORRHEA are the most common causes of epididymitis—*E. coli* in young boys and men over age 60; chlamydia and gonorrhea in men between ages 25 and 50. Repeated infections may result in permanent INFERTILITY.

Symptoms typically include scrotal PAIN and swelling, discharge from the PENIS, and difficulty urinating. Some men also experience FEVER, NAUSEA, and pain extending into the sides of the abdomen (the flank area). The diagnostic path includes examination to rule out TESTICULAR TORSION and culture of the discharge to identify the responsible PATHOGEN. Treatment is a course of the appropriate ANTIBIOTIC MEDICATIONS when the infection is bacterial. As with all infections, it is essential to complete the entire prescribed course of antibiotics even when symptoms improve. Less commonly, viruses (such as the MUMPS VIRUS) may cause epididymitis. Viral epididymitis resolves without treatment (antibiotic medications cannot treat viral infections).

The doctor may recommend ANALGESIC MEDICATIONS such as acetaminophen or NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs) such as ibuprofen to relieve discomfort and fever; NSAIDs can also relieve inflammation. Ice packs or cold cloths applied to the SCROTUM and supporting the scrotum such as by wearing an athletic supporter may also provide relief.

See also ABSCESS; [HEMATOSPERMIA](#); [ORCHITIS](#); SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; [URETHRITIS](#).

episiotomy A surgical incision through the tissues of the PERINEUM to extend the opening of the VAGINA during CHILDBIRTH. The most common types of episiotomy are the midline (median) incision, which extends from the vaginal opening toward the ANUS, and the mediolateral incision, which extends from the vaginal opening diagonally to either side. The obstetrician numbs the tissues of the perineum with an injected local anesthetic (if the woman does not already have epidural anes-

thetia), then makes the incision. After delivery of the baby and the PLACENTA, the obstetrician sutures (stitches) the incision closed.

Though once commonplace as a routine measure to prevent tearing of the vagina and surrounding tissues, episiotomy is now a procedure most obstetricians perform only when it appears that a natural tear will penetrate into the muscles of the perineum or RECTUM. The prevailing belief supporting preventive episiotomy had been that the clean cut of a surgical incision healed more rapidly and with fewer complications than the often jagged wound that occurred with a natural tear (also called a laceration). However, numerous studies have failed to support this premise, and the American College of Obstetricians and Gynecologists (ACOG) now advises against routine episiotomy.

Most episiotomies heal in four to six weeks though some women experience discomfort or PAIN for up to several months, especially with SEXUAL INTERCOURSE. Typically the obstetrician uses sutures the body absorbs as the incision heals. Risks of episiotomy include excessive bleeding, INFECTION, and weakening of the muscles of the pelvic floor that may result in URINARY INCONTINENCE, FECAL INCONTINENCE, and painful sexual intercourse. Many practitioners who provide care for women during PREGNANCY and childbirth advocate prenatal efforts, such as perineal massage to increase tissue elasticity and KEGEL EXERCISES to strengthen and tone the pelvic muscles; perineal massage during labor may also reduce the risk for natural tears and thus lower the likelihood for episiotomy.

See also [CESAREAN SECTION](#); [PRENATAL CARE](#); [SURGERY BENEFIT AND RISK ASSESSMENT](#).

erection The enlarged and hardened PENIS. Erections begin in the male fetus before birth and continue throughout life. An erection is necessary for SEXUAL INTERCOURSE and in an adult man usually occurs as a result of sexual arousal. Erections also occur spontaneously during sleep, usually during rapid eye movement (REM) sleep. A man typically has up to a half dozen nocturnal erections each night. Doctors do not know what causes nocturnal erections though believe they are a consequence of electrical activity in the BRAIN, not of sexual stimulation.

An erection during sexual arousal occurs as a result of interactions between the thoughts and physical stimulation of the penis. The sequence of interactions triggers the release of nitric acid, acetylcholine, EPINEPHRINE, and other neurotransmitters (biochemicals that conduct NERVE impulses). These substances cause the smooth MUSCLE tissue supporting the corpora cavernosa, the two tubelike channels along the top of the penis, to relax. BLOOD flows into the corpora cavernosa. Some of the layers of tissue within the penis contract to help hold the blood within the corpora cavernosa, and valves in the veins that normally carry blood from the penis close. These events cause the size of the penis to increase in length and circumference.

An erection may come to fullness within a few seconds to several minutes, depending on numerous factors such as the man's age and lasts generally until EJACULATION. Some men can sustain an extended erection during sexual activity. Nearly as quickly as the tissues of the penis release nitric acid, they also release the enzyme phosphodiesterase (PDE), which counters the actions of nitric acid and other neurotransmitters to allow blood to flow out of the penis. This action gains momentum after ejaculation or other culmination of sexual activity, serving to reverse the actions of these neurotransmitters. The penis again goes limp (becomes flaccid).

See also [CONTRACEPTION](#); [ERECTILE DYSFUNCTION](#); [FERTILITY](#); [MASTURBATION](#); [NEUROTRANSMITTER](#); [PARAPHIMOSIS](#); [PHIMOSIS](#); [PRIAPISM](#); [SEXUAL HEALTH](#); [VEIN](#).

erectile dysfunction The reduced ability or inability for a man's PENIS to become erect or sustain an erection adequate for SEXUAL INTERCOURSE. Erectile dysfunction, sometimes called impotence, may occur as a physiologic condition, psychologic or emotional condition, or combination. Most commonly, however, all of these factors contribute to the condition. About 25 million men in the United States have chronic (long-term) erectile dysfunction.

Physiologic causes of erectile dysfunction include

- NERVE damage that occurs as a complication of PROSTATECTOMY (surgery to remove the PROSTATE GLAND)

- DIABETES, which progressively damages the body's arteries and nerves
- peripheral NEUROPATHY, which may damage the nerves that supply the penis
- MULTIPLE SCLEROSIS, a degenerative neurologic disorder that causes loss of nerve function in various areas of the body
- ATHEROSCLEROSIS, which may occlude the arteries that serve the penis and slow the flow of BLOOD to the penis
- chronic LIVER disease or chronic kidney disease
- SPINAL CORD INJURY OR TRAUMATIC BRAIN INJURY (TBI), either of which may interrupt the flow of nerve impulses between the CENTRAL NERVOUS SYSTEM and the PERIPHERAL NERVOUS SYSTEM

Cigarette smoking is a key contributing factor for neuropathy and atherosclerosis, compounding the effect these conditions have throughout the body. Numerous medications may cause erectile dysfunction as an undesired SIDE EFFECT. The most common culprits are ANTIDEPRESSANT MEDICATIONS, antihypertensive medications to treat HYPERTENSION (high BLOOD PRESSURE), and ANTIHISTAMINE MEDICATIONS to treat seasonal allergies. Fear, stress, anxiety, and DEPRESSION are among the psychologic and emotional causes of erectile dysfunction.

ERECTILE DYSFUNCTION AND HEART DISEASE

Studies suggest erectile dysfunction in otherwise healthy men is a harbinger of HEART disease, notably ATHEROSCLEROSIS and CORONARY ARTERY DISEASE (CAD). The small arteries that flood the PENIS with BLOOD during ERECTION appear to show the effects of accumulated arterial plaque earlier than other arteries in the body. Though other arteries of similar size likely occlude to similar extent, men are more likely to notice and pay attention to circumstances that interfere with erection.

Symptoms and Diagnostic Path

The inability to get or sustain an adequate erection is the symptom of erectile dysfunction. The diagnostic path begins with a thorough physical examination, including DIGITAL RECTAL EXAMINATION (DRE) to assess the status of the prostate gland and blood tests to measure the levels of lipids (cholesterol

and triglycerides), TESTOSTERONE, GLUCOSE (fasting blood glucose), and liver enzymes. The doctor may desire additional diagnostic procedures, depending on the results of these preliminary tests. Such procedures may include Doppler ULTRASOUND to assess the flow of blood to and within the penis, testing of nerve function and reflexes, and other factors of function. Because a man normally experiences multiple erections during sleep, some tests are done when the man is sleeping (such as the nocturnal penile tumescence test), to measure the characteristics of nocturnal erections.

Treatment Options and Outlook

Treatment targets the underlying cause when it is identifiable. About 85 percent of erectile dysfunction results from physiologic causes. Sometimes treatment is straightforward and relatively easy, such as changing to a different medication when the cause of erectile dysfunction is medication side effect. Often, however, the most effective treatment addresses multiple contributing factors and encompasses medical interventions, lifestyle modifications, and psychologic therapy or counseling.

Medical interventions Phosphodiesterase (PDE) inhibitors, also called selective enzyme inhibitors, are the least intrusive and often most successful medical treatment for erectile dysfunction. The best known of these oral medications to treat erectile dysfunction is sildenafil, first marketed under the trade name Viagra. Other medications in this classification include vardenafil (Levitra) and tadalafil (Cialis). These drugs work by delaying the enzyme-initiated process through which an erection subsides, extending the erection. The erection still requires sexual stimulation to develop; these medications do not cause spontaneous erection. Men who take certain medications to treat HEART disease, such as some antihypertensive medications to treat high blood pressure, cannot take PDE inhibitors because the actions of the drugs are similar and combining them can cause fatally low blood pressure. PDE inhibitors are most effective in men who have mild to moderate vascular disease (such as atherosclerosis) or arterial damage due to diabetes.

Prescription-strength preparations of the herb-derived product YOHIMBE/YOHIMBINE also may extend erections though work through a different

mechanism. Yohimbe (the herb) and yohimbine (the active ingredient derived from the herb) products require a doctor's prescription in the United States because they act on the parasympathetic NERVOUS SYSTEM (a division of the autonomic nervous system that regulates certain involuntary functions). Yohimbe/yohimbine products are most effective in men who have mild to moderate neuropathy (nerve damage). The supplement arginine may also decrease erectile dysfunction by increasing nitric oxide.

Other medications that cause erection are self-injected into the penis or inserted as tiny suppositories (about the size of a grain of rice) into the urethral meatus (opening of the URETHRA at the tip of the penis). These medications contain alprostadil, a formulation of PROSTAGLANDINS, that instigates the sequence of events within the penis that cause it to engorge and stiffen. Unlike oral PDE inhibitors, these medications do cause erection regardless of sexual stimulation because they act directly on the smooth MUSCLE within the penis that causes the corpora cavernosa to relax and fill with blood. The primary drawback to these medications is their form of administration, which limits their appeal as well as the frequency with which a man may use them (no more often than once every five days).

Surgery to repair damaged blood vessels or insert penile implants is an option for erectile dysfunction that does not respond to medications. The most commonly used penile implants are a combination of inflatable tubes, a tiny pump, and small reservoirs that contain a sterile fluid. The man activates the pump, usually placed in the SCROTUM or at the base of the penis, to fill the

tubes to acquire an erection. A valve releases the fluid back into the reservoir.

Lifestyle modifications Lifestyle modifications such as weight loss, daily physical exercise, SMOKING CESSATION, and reduced ALCOHOL consumption can improve circulation and nerve function. Exercise in particular also helps reduce stress.

Psychologic therapy Counseling or sex therapy may be helpful when there are emotional factors at play. These factors may cause erectile dysfunction or develop because of it and then perpetuate it. Therapy may be individual or involve the sexual partner.

Risk Factors and Preventive Measures

Erectile dysfunction becomes more common after age 50. The key health risks for erectile dysfunction are cigarette smoking, OBESITY, diabetes, long-term ALCOHOLISM, CARDIOVASCULAR DISEASE (CVD), prostate disease, and kidney disease. Lifestyle significantly influences these factors. Lifestyle measures to reduce these risks include smoking cessation, nutritious EATING HABITS, daily physical exercise, moderation in or cessation of alcohol consumption, and weight management. Medical measures include management of blood lipid levels (cholesterol and triglycerides) and diligent control of blood glucose and INSULIN levels in men who have diabetes through appropriate medication therapy.

See also AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; BENIGN PROSTATIC HYPERPLASIA (BPH); DIET AND HEALTH; EXERCISE AND HEALTH; GENERAL ANXIETY DISORDER (GAD); PRIAPISM; PROSTATE HEALTH; SEXUAL HEALTH; WEIGHT LOSS AND WEIGHT MANAGEMENT.

fallopian tubes A pair of narrow enclosed channels that transport OVA (eggs) from the OVARIES to the UTERUS. The fallopian tubes extend from the top of the uterus, one on each side, curving downward to end just short of the ovaries. The ovary end of the fallopian tube is somewhat fluted with fringelike edges called the fimbriae. The fimbriae float in fluid. At OVULATION the ovary releases an ovum (egg) into the fluid. The fimbriae undulate, drawing the ovum into the fallopian tube. Tiny cilia (hairlike structures) project from the cells that form the tube's inner lining. The cilia move in wavelike motions that pull the ovum along the fallopian tube toward the uterus. If SPERM are present, they may fertilize the ovum on its journey through the fallopian tube. If no sperm are present, the ovum passes into the uterus and out of the body with MENSTRUATION.

A TUBAL LIGATION is a form of permanent CONTRACEPTION (birth control) in which the gynecologist ablates (destroys, such as by electrocautery) or cuts and ties the fallopian tubes to block passage for ova. Rarely, a tubal ligation may spontaneously reconnect. Recurrent infections such as SEXUALLY TRANSMITTED DISEASES (STDs) may affect the fallopian tubes, causing salpingitis or PELVIC INFLAMMATORY DISEASE (PID). Either may result in permanent loss of FERTILITY through scarring that obstructs (blocks) the fallopian tubes.

For further discussion of the fallopian tubes within the context of the structures and functions of reproduction and sexuality, please see the overview section "[The Reproductive System](#)."

See also INFERTILITY; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION.

family planning The process of intentional decision making around having children. Family plan-

ning encompasses choices in regard to PREGNANCY, ADOPTION, and not having children. Factors that influence family planning include general health, FERTILITY, personal preferences, religious beliefs, and lifestyle matters such as partnership status and work or career demands. In the United States about half of all pregnancies are intended. One million unintended pregnancies occur in teens. The US government's program of health goals HEALTHY PEOPLE 2010 calls for the availability of appropriate resources (such as education and contraceptive methods) so that all pregnancies are intended.

Planning pregnancy prevention (CONTRACEPTION) and pregnancy (conception) are equally important. More than a half dozen methods of contraception are available, from abstinence and cyclic timing (rhythm method) to sustained-release HORMONE regulation. The choice of contraception should consider availability, ease of use, rate of success, and personal preferences of sexual partners. The most common reason for failure of any given contraceptive method is failing to use it. However, the only certain method for preventing pregnancy is abstinence (not having SEXUAL INTERCOURSE). No other method of birth control is 100 percent certain to prevent pregnancy, though methods such as TUBAL LIGATION and VASECTOMY (operations to produce permanent sterilization) come close.

A key aspect of pregnancy planning is birth spacing—the amount of time between the births of children. From a health perspective, three years or more between births is optimal for both maternal and child health. This spacing allows the mother to fully recuperate between pregnancies as well as to provide the attention that each child needs. Siblings who have three or more years

between them are in different developmental stages for most of their childhood years, requiring different kinds of attention. Providing adequate attention to each child is more difficult when their ages are so close together that their needs are similar. Birth spacing requires either abstinence or some form of contraception between pregnancies to prevent unintended pregnancy.

People may choose adoption (acquiring legal responsibility for a nonbiologic child) as an option for resolving INFERTILITY or because they feel it is a personally desirable or socially responsible approach to creating a family. Other people may choose to have no children, opting instead to define family in other ways.

See also [ABORTION](#); [GESTATIONAL SURROGACY](#).

fertility The ability to conceive a PREGNANCY, and in women to also carry the pregnancy to term. Men and women both become fertile during PUBERTY, when sexual maturity results in the development of SECONDARY SEXUAL CHARACTERISTICS. Men remain fertile all of their lives and are fertile on a continuous basis; women remain fertile through their late 40s or until MENOPAUSE and are fertile on a cyclic, monthly basis.

Female Fertility: Ovulation, Conception, and Pregnancy

Within a narrower context, fertility is the period of time within a woman's MENSTRUAL CYCLE when she is physiologically capable of CONCEPTION. This period of time is the approximately 48 hours before and 24 hours after OVULATION (release of an ovum). The ovum remains receptive to fertilization during the time it travels through the fallopian tube on its way to the UTERUS. SPERM can survive 48 to 72 hours after entering the woman's reproductive tract (such as with SEXUAL INTERCOURSE). A woman can conceive when viable sperm are present in her body when she ovulates.

Knowing the precise timing of ovulation is difficult because it varies somewhat from one menstrual cycle to another. As well, physical illness, trauma, or surgery can affect ovulation and fertility. Several methods may help a woman estimate when she is ovulating. The easiest, though the least precise, is counting 14 days back from the anticipated first day of MENSTRUATION. The days fer-

tility is most likely are 12, 14, and 16 days before the onset of menstruation. This method is imprecise because many women ovulate earlier or later than 14 days and experience variation from one menstrual cycle to another. Other methods may detect when ovulation occurs but cannot predict it before the fact.

The simplest device-oriented measure to estimate a woman's fertile time is basal body temperature. This is the first temperature of the day, taken before getting out of bed and with minimal movement. A woman's body temperature is up to one degree higher after ovulation than before ovulation. The beginning of the rise marks ovulation. Either a regular oral thermometer or a basal body thermometer (which registers only between 96°F and 100°F) works for this purpose. Combining basal body temperature with calendar timing is more accurate than either method alone.

Home ovulation tests may examine saliva or URINE. The urine test, which has been available since the mid-1980s, detects the presence of LUTEINIZING HORMONE (LH) in the urine. The PITUITARY GLAND releases LH to stimulate the luteal, or secretory, phase of the menstrual cycle and the ultimate release of the ovum. The LH test is similar to a home pregnancy test in that the sample of urine causes a change in the indicator when LH is present in the urine. The saliva test, which became available in 2002, allows examination of the saliva for changes in the concentration of potassium chloride. The amount of potassium chloride in the saliva increases during the luteal phase, a reaction to the surge of ESTROGENS that precedes ovulation. The saliva test uses a small microscope, which comes with the test kit, to examine a drop of saliva on a slide for the pattern of potassium chloride. Small spots are normal; fernlike patterns suggest ovulation.

The final element of fertility in women is the ability to sustain pregnancy through birth. Some conceptions are unable to implant, perhaps because of extensive UTERINE FIBROIDS, excessively tipped uterus, malformation of the uterus, and other circumstances in which the uterus cannot support the blastocyst. As many as a third of pregnancies spontaneously abort (miscarry) within the first eight weeks. Spontaneous ABORTION becomes less common after the 14th week.

Though a woman retains fertility for as long as she ovulates and has menstrual cycles (even if irregular), her fertility diminishes as she approaches menopause. Menstrual cycles and ovulation often become irregular in timing, and anovulatory cycles (menstrual cycles without ovulation) become more common. Other factors that influence fertility in women include

- oral contraceptives (birth control pills), which override the body's hormonal regulation of the menstrual cycle, or estrogen suppression therapy, such as to treat severe uterine fibroids or ENDOMETRIOSIS
- TURNER'S SYNDROME
- PREMATURE OVARIAN FAILURE (POF), in which the OVARIES stop functioning before natural menopause
- TUBAL LIGATION (surgery to "tie" or cut the FALLOPIAN TUBES as a permanent form of CONTRACEPTION)
- HYSTERECTOMY (surgery to remove the uterus)
- chronic PELVIC INFLAMMATORY DISEASE (PID), which may SCAR and block the fallopian tubes
- CHEMOTHERAPY OR RADIATION THERAPY to treat cancer anywhere in the body

Male Fertility and Conception

Male fertility relies on the motility (movement and thrust), morphology (physiologic form), and volume of sperm present in the ejaculate (SEMEN that leaves the man's PENIS with EJACULATION). Laboratory examination of a sperm sample measures these and other factors; there are no home tests for sperm viability. Sperm can live about 72 hours in the woman's reproductive tract, though the environment of the VAGINA is particularly hostile, and about half of the 500 million or so sperm typically present in a fertile man's ejaculate die during their passage through the it. However, dead and dying sperm are important to fertility because they provide protection and support for living, motile sperm. Dead sperm help form a protective barrier around surviving sperm. The movement of dying sperm helps propel onward the cluster of sperm that remain viable.

One healthy, functioning testicle is adequate to produce enough sperm for fertility. Though a man

remains fertile all his life the quality of his sperm (motility, morphology, and other characteristics) tends to decline in his later years (age 70 and older). This may become an issue in regard to fertility if the woman's fertility is marginal. Other factors that influence male fertility include

- inflammatory damage to the TESTICLES due to bacterial or viral INFECTION
- RETROGRADE EJACULATION (semen enters the BLADDER instead of leaving the penis during ejaculation)
- PROSTATECTOMY (surgery to remove the PROSTATE GLAND)
- VASECTOMY (surgery to clip or cut the VAS DEFERENS as a means of permanent contraception) or ORCHIECTOMY (surgery to remove a testicle)
- CRYPTORCHIDISM (undescended testicle), particularly bilateral or delayed diagnosis
- ERECTILE DYSFUNCTION
- chemotherapy or radiation therapy for cancer anywhere in the body

Body temperature also affects male fertility. Normally the SCROTUM (saclike structure that contains the testicles) rises and lowers to maintain ideal temperature for spermatogenesis (production of new sperm). FEVER, sitting in a hot tub, and wearing clothing that holds the scrotum tight against the body are factors that can raise the temperature in the testicles to one at which sperm cannot survive. Though these often are temporary factors, they may be permanent.

See also [AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; ASSISTED REPRODUCTIVE TECHNOLOGY \(ART\); STILLBIRTH.](#)

fetus The stage of prebirth development from nine weeks of gestation to birth. The organ systems and major structures take form during the EMBRYO stage, which encompasses the second to the eighth weeks of gestation. During the fetal stage, which is 32 weeks in a full-term PREGNANCY, the systems, organs, and structures grow and develop further sophistication in preparation for independent life. The fetus reaches viability (possibility of surviving on its own) at around 24 weeks of gestation.

HIGHLIGHTS OF FETAL GROWTH		
Fetal Age (Gestational Weeks)	Fetal Size	Key Developments
14	3 inches in length	face clearly formed LIVER produces erythrocytes
18	6 inches in length	lanugo (fine HAIR) on head movement may be detectable sucking gastrointestinal tract produces meconium
24	11 inches in length one pound in weight	viability possible with intensive medical care movement apparent eyebrows and eyelashes fingerprints and footprints heartbeat detectable with stethoscope gender detectable with ULTRASOUND startle REFLEX
28	15 inches in length two to three pounds in weight	viability possible eyelids open and close increasing level of BRAIN and NERVOUS SYSTEM functions alveoli in LUNGS
32	17 inches in length four pounds in weight	viability probable body fat BREATHING movements in lungs
36	19 inches in length five to six pounds in weight	viability likely fingernails completely cover fingertips head hair replaces lanugo on head
40	20 to 21 inches in length seven to eight pounds in weight	viable, full term body lanugo disappears lungs mature

See also [ABORTION](#); [CHILDBIRTH](#); [CONCEPTION](#); FETAL ALCOHOL SYNDROME; [PRENATAL CARE](#); [STILLBIRTH](#).

fibroadenoma A benign (noncancerous) tumor of the BREAST composed of a mix of fibrous and glandular tissues. Fibroadenoma is the most common benign breast tumor and most often develops in women under age 30. Researchers do not know what causes fibroadenoma. Many women who develop fibroadenomas have higher than normal

levels of ESTROGENS in their BLOOD circulation, though researchers do not know the extent to which this contributes. Fibroadenomas tend to grow during PREGNANCY and shrink after MENOPAUSE, supporting at least some level of hormonal involvement.

Most often the woman detects fibroadenoma as a lump she feels in her breast during BREAST SELF-EXAMINATION (BSE) or the doctor finds the fibroadenoma during the breast exam portion of the

woman's ROUTINE MEDICAL EXAMINATION. Fibroadenomas are characteristically firm, smooth, oval or round, and rubbery in texture. They move freely (are not attached to any surrounding tissues). Biopsy is the only means of definitive diagnosis. MAMMOGRAM is often not helpful in women under age 30 because their breast tissue is quite dense, which makes it difficult to distinguish growths within the breast. As well, the radiologic characteristics of fibroadenoma are very similar to those of breast cysts and BREAST CANCER. ULTRASOUND imaging is sometimes useful to visualize the growth though does not provide definitive diagnosis either.

Some doctors recommend surgery to remove a fibroadenoma because although fibroadenoma does not evolve into cancer, there is a slight possibility cancer may develop within the epithelial cells the fibroadenoma contains. Other doctors suggest a course of watchful waiting when the diagnosis is certain and the fibroadenoma is small. About 10 percent of fibroadenomas spontaneously disappear within a year or two of their discovery. Should the fibroadenoma grow or change, the doctor may biopsy it again or remove it.

See also FIBROCYSTIC BREAST DISEASE.

fibrocystic breast disease A chronic condition in which multiple noncancerous cysts develop in the breasts. As the cysts rupture and heal, they cause clusters of scarlike tissue that form palpable lumps in the BREAST. Though called a disease, this condition is benign (harmless and noncancerous) and very common, affecting more women than not; doctors consider it a normal process associated with the fluctuation of hormones during the MENSTRUAL CYCLE. Fibrocystic breast disease commonly affects both breasts though may affect only one breast.

The health concerns of fibrocystic breast disease are twofold. First, the cysts often cause PAIN and swelling of the breasts, particularly in the week before and the first day or two of the menstrual period. Second, it is not possible to be certain a breast lump is a cyst, raising concerns about BREAST CANCER. As well, though the cysts themselves do not become cancerous, when they are abundant their presence can delay detection of a

breast cancer tumor. Fibrocystic breasts are more dense, decreasing the effectiveness of the MAMMOGRAM.

Symptoms and Diagnostic Path

Fibrocystic breasts are typically painful. The discomfort may be persistent, having the quality of dull aching or a sensation of fullness, or cyclic tenderness that intensifies the week before and first few days of the menstrual period. Other symptoms may include

- bumpy or lumpy texture to one quadrant, one side, or all of the breast
- itching or tingling of the nipples
- premenstrual swelling of the breasts

Fibrocystic lumps are characteristically rubbery, smooth, and rounded. With palpation they move within the breast; they are not anchored to the underlying structure of the breast. The diagnostic path includes comprehensive palpation of the breasts. Depending on the woman's age, health history, risk for breast cancer, and other factors, the doctor may use diagnostic imaging procedures such as mammogram and breast ULTRASOUND to obtain additional information about the shape, size, and pattern of the fibrocystic tissue. The doctor may also biopsy several lumps to evaluate their pathology (cell structure and organization) and rule out other causes for the symptoms.

Treatment Options and Outlook

Lifestyle treatments that help mediate discomfort include wearing a supportive bra when symptoms are most significant. Some women get relief by limiting their intake of dietary fats and CAFFEINE, though clinical studies of the correlations between these factors and fibrocystic breasts so far have produced inconclusive and sometimes conflicting findings. Others find that vitamin E, vitamin B₆ (pyridoxine), and the herbal preparation evening primrose oil reduce tenderness and swelling. Medical interventions that may provide relief include NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), which reduce INFLAMMATION, and oral contraceptives (birth control pills), which regulate the hormonal cycle. Nearly always the discomforts of

fibrocystic breasts abate with MENOPAUSE and the lumpiness of the breasts diminishes, though some fibrocystic tissue remains.

Risk Factors and Preventive Measures

There are no clear risk factors or measures to prevent fibrocystic breast disease. It is important for

women who have fibrocystic breasts to be diligent in performing monthly BREAST SELF-EXAMINATION and to see their health-care providers when they detect any changes in their breasts.

See also [BREAST HEALTH](#); [ENDOMETRIOSIS](#); MEDICINAL HERBS AND BOTANICALS; [UTERINE FIBROIDS](#); VITAMINS AND HEALTH.



genitalia The collective term for the organs and structures of reproduction, also called the sex organs or the genitals.

Male genitalia The external male genitalia are the PENIS and SCROTUM; the internal male genitalia are the URETHRA, TESTICLES, VAS DEFERENS, bulbourethral glands (also called Cowper's glands), ejaculatory ducts, seminal vesicles, spermatic cords, and PROSTATE GLAND. All structures of the internal male genitalia occur in pairs except the prostate gland and urethra.

Female genitalia The female external genitalia are the mons pubis, labia majora, labia minora, CLITORIS, Skene's glands, Bartholin's glands, hymen, and vaginal introitus. Collectively the female external genitalia are the VULVA or pudendum. The female internal genitalia are the OVARIES, FALLOPIAN TUBES, UTERUS, CERVIX, and VAGINA.

For further discussion of the genitalia within the context of the structures and functions of reproduction and sexuality, please see the overview section "[The Reproductive System](#)."

See also [CHILDBIRTH](#); [CONCEPTION](#); [PREGNANCY](#); [SEXUAL HEALTH](#); [SEXUAL INTERCOURSE](#).

genital trauma Injury to the GENITALIA (organs and structures of reproduction). Genital trauma may occur as the result of accidental injury, ritual genital mutilation, or SEXUAL ASSAULT and may affect the external or internal genitalia. Genital trauma may result in PAIN, structural damage, impaired genitourinary function, SEXUAL DYSFUNCTION, and INFERTILITY.

Male Genital Trauma

Common forms of genital trauma in young boys are in straddle injuries (such as falling onto the bar of a bicycle), blunt force injuries to the groin

(such as being struck with a thrown or kicked ball), and toileting injuries (such as the toilet seat falling onto the PENIS or getting the penis or SCROTUM caught in the pants zipper).

In older boys and teens, blunt force injuries are more common. Most organized athletic activities and sports require boys to wear a protective cup to guard against such injuries. In adult men, genital trauma may occur as a result of blunt force and during sexual activity that places unusual or excessive pressure on the erect penis or on the scrotum and TESTICLES.

Some people and organizations that oppose routine male infant CIRCUMCISION (surgical removal of the foreskin) view its practice as a form of male ritualistic genital mutilation.

Female Genital Trauma

Straddle-type injuries are common in young girls, though less frequently from bicycles and more often from activities such as gymnastics and horseback riding. Activities that result in the "splits," whether intentional or accidental, can cause significant bruising and tearing of the external genitals and the PERINEUM (region between the opening of the VAGINA and the ANUS).

Sexual assault is a frequent cause of genital trauma in older girls and women, often resulting from rape (forced, nonconsenting, and violent SEXUAL INTERCOURSE). Health-care providers tend to view most circumstances of female genital trauma with the suspicion that they could represent sexual abuse or assault, in part because it is often the case and in part because the laws in many communities in the United States require them to do so. Hospitals and health-care providers must follow specific procedures to preserve potential evidence when treating sexual assault victims.

Women may experience genital trauma during **CHILDBIRTH**, particularly with vaginal delivery of a breech presentation (baby born bottom first) or a large baby. Some women have birth-related traumatic tearing of the perineum, and others have episiotomy in an attempt to limit the extent of trauma or enlarge the vaginal opening to allow the baby to pass. The resulting injuries may require surgical repair and sometimes result in long-term complications affecting urinary continence, fecal continence, and pleasure during sexual intercourse.

Female ritual genital mutilation, also called female circumcision, remains common in some cultures despite widespread opposition from the World Health Organization (WHO), Amnesty International, and other health and human rights organizations worldwide. Within such cultures ritual genital mutilation may be a rite of passage, a mark of ownership, or a religious practice conducted in early childhood by nonmedical practitioners, without **ANESTHESIA** and often under unsanitary conditions. Complications are common and often severe. WHO and other organizations have made it a goal to eliminate ritual genital mutilation worldwide.

See also **PRAPISM**; **TESTICULAR TORSION**; **VULVODYNIA**.

gestational diabetes The development of **INSULIN RESISTANCE** or type 2 **DIABETES** during **PREGNANCY**. Gestational diabetes develops between 24 and 28 weeks of pregnancy. Doctors believe the rising levels of hormones the **PLACENTA** produces at this point in pregnancy interfere with the ability of the woman's body to properly metabolize **INSULIN**. Insulin production remains normal. Diabetes that manifests earlier than 24 weeks in pregnancy is nearly always diabetes that was undetected at the start of the pregnancy. Gestational diabetes goes away shortly after delivery, though women who have gestational diabetes have increased risk for developing type 2 diabetes later in life.

Untreated gestational diabetes poses a health risk primarily for the **FETUS**. The excessive **GLUCOSE** (sugar) that circulates in the mother's **BLOOD** crosses the placenta. When it reaches the fetus the excessive glucose fuels fetal growth, resulting in fetal size up to 20 percent greater than normal.

This growth becomes problematic within the **UTERUS** as the fetus cannot move as freely. Adequate prenatal movement is important for proper muscular development. A fetus larger than about eight pounds often has difficulty passing through the birth canal. The circumstance of an overly large fetus, called **macrosomia**, often necessitates birth by **CESAREAN SECTION** (surgical delivery) to safeguard the health of both baby and mother. As well, the newborn infant may experience **HYPOGLYCEMIA** (low blood glucose) in the first hours after birth.

Symptoms and Diagnostic Path

Most often gestational diabetes has few noticeable symptoms. When symptoms do occur they may include frequent **URINATION**, increased thirst, and increased hunger. Because these are common in pregnancy, however, they are difficult to distinguish as symptoms of diabetes. Routine **URINE** tests at each prenatal doctor visit screen for the overflow of glucose in the urine, which indicates high blood glucose. Health-care providers routinely test for elevated glucose in the woman's blood circulation between the 24th and 28th weeks of pregnancy. The most common such test is the three-hour glucose tolerance test. Findings of an elevated blood glucose level at two or more of the four drawings of blood over the course of the test generally establishes the diagnosis of gestational diabetes.

Treatment Options and Outlook

Many women are able to manage gestational diabetes through nutritional **EATING HABITS** and daily exercise. Women for whom lifestyle measures do not maintain stable blood glucose levels typically require insulin injections through the remainder of pregnancy. The safety of oral antidiabetes medications in pregnancy remains undetermined, though some doctors offer this treatment. Diligent management of blood glucose levels helps maintain normal growth and weight of the fetus.

In nearly all women gestational diabetes goes away within a week of delivery and for a third of women diabetes is never again a health concern. However, in some women who have high risk for diabetes in the first place gestational diabetes may persist to become conventional diabetes. One in

five women who has gestational diabetes will develop conventional diabetes within five years of her baby's birth, and about two thirds of women will develop the condition later in life.

Risk Factors and Preventive Measures

Any pregnant woman can develop gestational diabetes. Factors that increase the risk for gestational diabetes include

- gestational diabetes in a previous pregnancy
- obesity
- African American or Hispanic heritage
- age 25 or older

Because gestational diabetes results from the effects in the woman's body of hormones the placenta produces, there are no certain measures to prevent its development. Lifestyle measures to maintain nutritious eating habits, daily exercise, and healthy weight help the body use glucose and insulin as efficiently as possible.

See also [ECLAMPSIA](#); [LIFESTYLE AND HEALTH](#); [PREECLAMPSIA](#); [WEIGHT LOSS AND WEIGHT MANAGEMENT](#).

gestational hypertension See [PREECLAMPSIA](#).

gestational surrogacy A circumstance in which one woman carries a PREGNANCY for another woman who cannot carry it herself. Gestational surrogacy is among the possible solutions for INFERTILITY, typically in circumstances such as uterine malformation that prevent successful implantation or carrying the pregnancy to term.

The woman who carries the pregnancy is the gestational surrogate or gestational carrier; the woman to whom the pregnancy belongs is the intended parent. The gestational surrogate may be a relative of or a woman or couple desiring the pregnancy, may know the woman or couple desiring the pregnancy, or may make herself available to a FERTILITY clinic for the purpose of gestational surrogacy. The pregnancy takes place through

some form of ASSISTED REPRODUCTIVE TECHNOLOGY (ART), typically in vitro fertilization. ART may use the intended mother's egg, a donor egg, or the gestational surrogate's egg fertilized with the intended father's SPERM or donor sperm. As with any pregnancy, multiple factors affect the success of these efforts.

Gestational surrogacy entails intense emotional and legal complexities as well as physical and health risks for the gestational surrogate. Women considering gestational surrogacy, whether as intended parent or gestational surrogate, should obtain legal advice before initiating the process. It is crucial for all participants to fully understand the risks and to agree, via written contract, to the conditions of the arrangements. In the United States each state determines the legal status of surrogacy; many states restrict financial arrangements with and payments to gestational surrogates as well as tightly regulate the myriad aspects of legal parentage and responsibility. Though gestational surrogacy is often a positive experience for all involved, the potential for complications and problems exists.

See also [ADOPTION](#); [FAMILY PLANNING](#).

gynecomastia BREAST enlargement in a man. Gynecomastia may be a symptom of OBESITY or hormonal imbalance such as may occur during PUBERTY or with various endocrine disorders that affect the production of TESTOSTERONE. Advanced CIRRHOSIS, LIVER CANCER, and chronic ALCOHOLISM often produce gynecomastia because the resulting dysfunction of the LIVER alters how the adipose (fat) cells metabolize ESTROGENS. Estrogen levels in the BLOOD circulation tend to rise with chronic liver disease or damage to the liver. Gynecomastia is also a characteristic SIDE EFFECT of HORMONE THERAPY to treat PROSTATE CANCER, again because the balance of estrogen in the blood circulation increases. Treatment for gynecomastia depends on the underlying cause.

See also [MASTALGIA](#).



hematospermia BLOOD in the SEMEN that may be apparent with EJACULATION. Trauma and INFECTION are the main causes of hematospermia. SEXUALLY TRANSMITTED DISEASES (STDs), notably GONORRHEA and CHLAMYDIA, are common infections that irritate and inflame the URETHRA, often causing bleeding into both the URINE (HEMATURIA) and the semen as either passes through the urethra to leave the body. Less common causes of hematospermia include bleeding disorders (health conditions or medication induced); severe HYPERTENSION (high BLOOD PRESSURE); and, in men over age 50, PROSTATE CANCER. Diagnostic and therapeutic efforts focus on identifying and treating the underlying cause.

See also EPISTAXIS; URETHRITIS.

hot flashes Sudden episodes of flushing and sweating that occur with the fluctuating HORMONE levels that precede MENOPAUSE or as a consequence of HORMONE THERAPY such as to treat HORMONE-DRIVEN CANCERS. Though researchers do not know the precise mechanisms of hot flashes, they believe the sudden drops in ESTROGENS affect the thermoregulatory centers in the BRAIN that cause the body to function as though it must reduce body temperature. SKIN flushing and sweating are among the methods the body uses to accomplish such reduction. Hot flashes associated with menopause improve and usually go away when the body's estrogen levels stabilize.

Lifestyle measures to mitigate the discomfort of hot flashes include dressing in layers to allow rapid cooling, drinking cool fluids at the onset of a hot flash, minimizing CAFFEINE consumption, and avoiding foods that are high in tyramines, including red wine, aged cheese, smoked meats, and concentrated yeasts such as miso. Medical treatments for hot flashes include selective serotonin

reuptake inhibitor (SSRI) medications, a classification of antidepressant medication that appears to reduce the frequency and intensity of hot flashes, or short-term hormone replacement therapy (HRT). Alternative and complementary approaches to relieve hot flashes include ACUPUNCTURE and botanical remedies such as BLACK COHOSH and soy.

See also ANTIDEPRESSANT MEDICATIONS; MEDICINAL HERBS AND BOTANICALS; PREMATURE OVARIAN FAILURE (POF).

hydrocele A fluid-filled growth, similar to a cyst, that develops in the SCROTUM. Most hydroceles are congenital (present at birth) and occur as a result of incomplete closure of the channel through which the testicle descends from the abdomen to the scrotum. The defect allows peritoneal fluid to seep from the abdominal cavity into the scrotum. A congenital hydrocele, also called a primary hydrocele, appears as a variable and usually painless enlargement of the scrotum. The size of the enlargement may fluctuate with changes in abdominal pressure, increasing with activities such as bearing down (Valsalva maneuver), coughing, sneezing, or, in infants, vigorous crying. Secondary hydrocele may develop after viral INFECTION (more common in children) or trauma to the scrotum.

The preliminary diagnosis of hydrocele is clinical, based on the scrotum's translucency. In this simple test the doctor holds a bright, focused penlight against the side of the scrotum. When the cause of scrotal swelling is hydrocele, the light passes uniformly through the tissues of the scrotum. Most other causes of scrotal swelling are not translucent. An OPERATION to repair a primary hydrocele is the treatment of choice; surgical

examination of the swelling subsequently confirms the diagnosis. The operation closes the defect that allows fluid to seep into the scrotum. Complications after surgery are rare though could include anesthetic reaction, unusual bleeding, or infection. Secondary hydrocele generally heals on its own.

See also [HERNIA](#); [TESTICLES](#); [VIRUS](#).

hypogonadism Dysfunction of the gonads resulting in inadequate production of sex hormones. In men the [TESTICLES](#) (also called testes) are the gonads that produce [ANDROGENS](#) and in women the [OVARIES](#) are the gonads that produce [ESTROGENS](#). In primary hypogonadism the ovaries or testicles themselves fail. Genetic reasons for such failure are [TURNER'S SYNDROME](#) in females and [KLINEFELTER'S SYNDROME](#) in males. These genetic disorders result from errors in the sex chromosomes.

Hypogonadism may also be central, a result of problems with the endocrine mechanisms that regulate the function of the ovaries or testicles. The most common of such problems are traumatic injury, surgery, [RADIATION THERAPY](#), and [CHEMOTHERAPY](#). Tumors of the [PITUITARY GLAND](#), untreated [HYPOTHYROIDISM](#), and [EATING DISORDERS](#) such as [anorexia nervosa](#) that result in severe [NUTRITIONAL DEFICIENCY](#), may also cause central hypogonadism.

Symptoms of hypogonadism depend on the developmental stage of the individual. Primary hypogonadism that occurs in childhood, such as resulting from Turner's syndrome or Klinefelter's syndrome, causes absence of [PUBERTY](#) and failure to develop [SECONDARY SEXUAL CHARACTERISTICS](#). Hypogonadism that develops in adulthood results in menopausal symptoms such as [HOT FLASHES](#) in women and diminished [LIBIDO](#), [ERECTILE DYSFUNCTION](#), and sparsity of facial [HAIR](#) in men.

The diagnostic path includes [BLOOD](#) tests to measure blood levels of estrogen, [TESTOSTERONE](#), [FOLLICLE-STIMULATING HORMONE \(FSH\)](#), [LUTEINIZING HORMONE \(LH\)](#), and thyroid hormones. Treatment for primary hypogonadism in most situations is [HORMONE THERAPY](#) to restore blood levels of the sex hormones to normal levels for the person's age. When hypogonadism is central, treatment targets the underlying cause. Hormone therapy initiates puberty when hypogonadism occurs in childhood. However, [FERTILITY](#) issues may remain even with

treatment though other symptoms typically improve.

See also [CHROMOSOMAL DISORDERS](#); [CHROMOSOME](#); [GYNECOMASTIA](#); [HORMONE](#); [SEX CHROMOSOME](#); [THYROID GLAND](#).

hysterectomy A surgical OPERATION to remove the [UTERUS](#). Hysterectomy may be treatment for [ENDOMETRIAL CANCER](#) or for noncancerous conditions that cause significant symptoms and do not respond to less invasive treatments. Among such conditions are [UTERINE FIBROIDS](#), [UTERINE PROLAPSE](#), [DYSFUNCTIONAL UTERINE BLEEDING \(DUB\)](#), and [ENDOMETRIOSIS](#). Whatever its reason, a consequence of hysterectomy is immediate loss of [FERTILITY](#). Hysterectomy is the second-most common operation women undergo in the United States; [CESAREAN SECTION \(surgical CHILDBIRTH\)](#) is the most common. Surgeons in the United States perform more than 600,000 hysterectomies each year.

Surgical Procedure

The [ANESTHESIA](#) for hysterectomy may be regional, such as epidural block, with sedation or general (deep sleep). The choice of anesthesia depends on the type of hysterectomy the woman is having, the woman's preferences, and the recommendations of the surgeon and anesthesiologist.

A simple hysterectomy removes only the uterus (sometimes called a supracervical hysterectomy); a total hysterectomy removes the uterus and [CERVIX](#). Both operations leave the [OVARIES](#) in place to continue providing hormones that carry the woman to a natural [MENOPAUSE](#) if she has not already reached that stage of her life. Radical hysterectomy may be necessary when endometrial cancer or [CERVICAL CANCER](#) is the reason for the operation. In radical hysterectomy the surgeon removes the uterus, cervix, and upper [VAGINA](#) along with much of the tissue that supports these structures.

The operation may be an [OPEN SURGERY](#), in which the surgeon makes a long incision through the [SKIN](#) and layers of [MUSCLE](#) to expose the uterus, or laparoscopically assisted vaginal hysterectomy, in which the surgeon removes the uterus through multiple small incisions in the abdomen and vagina and removes the uterus with the aid of a lighted, magnifying laparoscope that displays the pelvic structures on a monitor. A laparoscopically

assisted vaginal hysterectomy is somewhat more complex for the surgeon to perform though significantly faster recovery for the woman. It is an appropriate option when hysterectomy is to treat noncancerous conditions.

A laparoscopically assisted vaginal hysterectomy generally requires no more than an overnight stay in the hospital the night after the surgery. A woman often can return to regular activities in about six weeks with the laparoscopic operation. The typical hospital stay for open hysterectomy is three to five days, with full recovery and recuperation in about eight weeks.

Risks and Complications

The primary risks associated with hysterectomy are possible excessive bleeding, BLOOD clots, and INFECTION. Complications may include damage to the nerves that control the bowel or BLADDER that results in FECAL INCONTINENCE or URINARY INCONTINENCE or damage to the structure of the bladder or ureters (tubelike structures that drain URINE from the KIDNEYS to the bladder). These complications are uncommon though may have long-term consequences. When the surgeon leaves the FALLOPIAN TUBES and ovaries intact, these structures sometimes atrophy (shrink). Women who have total hysterectomies with removal of the cervix sometimes experience PAIN during SEXUAL INTERCOURSE for the first few months after surgery. Women who have hysterectomies tend to enter menopause somewhat earlier even when they retain their ovaries.

Outlook and Lifestyle Modifications

Most women return to full, regular activities within two months of surgery (and many sooner). Hysterectomy means the end of MENSTRUATION (though not necessarily the start of menopause), which is sometimes an emotional adjustment. The relief of symptoms related to the condition that necessitated the hysterectomy is sometimes pro-

found, allowing the woman to return to a lifestyle and activities that she had long enjoyed but had stopped participating in because of the symptoms. In circumstances other than cancer, it is important for a woman to understand the nonsurgical options that are available to treat her condition so she can make a fully informed decision.

See also CANCER TREATMENT OPTIONS AND DECISIONS; OOPHORECTOMY; SEXUAL HEALTH; SURGERY BENEFIT AND RISK ASSESSMENT.

hysteroscopy A diagnostic or therapeutic procedure to examine the interior of the UTERUS using a lighted magnifying endoscope. Hysteroscopy is an outpatient surgical procedure that requires regional or general ANESTHESIA. After the administration of anesthesia the gynecologist dilates the CERVIX and inserts the lighted, flexible tube of the hysteroscope into the uterus and fills the uterus with carbon dioxide gas or sometimes liquid saline solution to push the uterine walls apart.

The hysteroscope allows the gynecologist to closely examine the entire endometrium (lining of the uterus) and the entries to the FALLOPIAN TUBES. The gynecologist may use the hysteroscope to obtain tissue samples for biopsy, remove UTERINE FIBROIDS or polyps, and repair minor injuries to the wall of the uterus and certain congenital malformations such as uterine septum.

The risks of hysteroscope include those of anesthesia as well as INFECTION, excessive bleeding, and uterine perforation (puncture of the uterine wall). These risks are uncommon though may require further treatment. Infection requires treatment with ANTIBIOTIC MEDICATIONS. Uterine perforation usually heals on its own. Excessive bleeding may require medications or follow-up surgery to control. Minor bleeding and discomfort (cramping) are normal after hysteroscopy and may continue for a few days.

See also COLPOSCOPY; ENDOSCOPY; SURGERY BENEFIT AND RISK ASSESSMENT.

infertility The inability to conceive or maintain a PREGNANCY. Infertility may be transitory (relate to a specific set of circumstances), treatable, or permanent. Infertility affects about 10 percent of Americans who attempt pregnancy.

There are numerous possible causes of infertility that can affect any of the various stages in the process of CONCEPTION. Causes may affect the woman, the man, or the couple in equal distribution. One of the most significant is the woman's age. An increasing number of women in the United States delay starting their families until completing their education and establishing their careers, the average age of first pregnancy is age 30. Though a woman can remain fertile into her late 40s, the likelihood of conception appreciably diminishes each year after age 35.

Infertility is highly emotional for most people. Infertility often comes as a shock, particularly for younger people who had no reason to suspect they were not fertile. Some people feel guilt or regret about choices made earlier in life in regard to CONTRACEPTION and FAMILY PLANNING. Diagnostic procedures and treatment approaches can be invasive and expensive and are without assurances. Though ASSISTED REPRODUCTIVE TECHNOLOGY (ART) is highly advanced and makes pregnancy possible for thousands of couples every year, it nonetheless is unable to help two thirds of couples who cannot conceive.

Female factor infertility In female factor infertility the reason for infertility rests with the woman. A third of infertility circumstances arise from female factors. Ovulatory dysfunction is the most common of them and may result from age, genetics, health conditions, or medical treatments. Blocked FALLOPIAN TUBES are also common. Previous ECTOPIC PREGNANCY, abdominal or pelvic sur-

gery, and complications from untreated SEXUALLY TRANSMITTED DISEASES (STDs) may SCAR and otherwise damage the fallopian tubes. Congenital anomalies of the reproductive organs, such as malformations of the UTERUS, may prevent implantation. EATING DISORDERS such as anorexia nervosa and OBESITY influence the body's endocrine functions and OVULATION. Cigarette smoking, excessive ALCOHOL consumption, and substance abuse also affect FERTILITY.

FEMALE INFERTILITY FACTORS

age over 35	excessive ALCOHOL use
anorexia nervosa	CHEMOTHERAPY
cigarette smoking	CUSHING'S SYNDROME
DIABETES	ENDOMETRIOSIS
OBESITY	OVARIAN CYST
PELVIC INFLAMMATORY DISEASE (PID)	PITUITARY GLAND dysfunction
PREMATURE OVARIAN FAILURE (POF)	POLYCYSTIC OVARY SYNDROME (PCOS)
RADIATION THERAPY	previous ECTOPIC PREGNANCY
substance abuse	SICKLE CELL DISEASE
untreated HYPOTHYROIDISM	TURNER'S SYNDROME
uterine malformations	UTERINE FIBROIDS

Male factor infertility In male factor infertility the reason for infertility rests with the man. A third of infertility circumstances arise from male factors. Male infertility factors may result from problems with spermatogenesis (production of SPERM), SEMEN production, ERECTION and EJACULATION, sperm count, sperm morphology (structure), and sperm motility (movement). Body temperature and scrotal temperature are crucial for spermatogenesis and sperm survival. Circumstances that prevent the SCROTUM from dropping, such as tight clothing, or sustained exposure to heat, such

as sauna or hot tub use, may affect sperm viability. Such effects may be temporary or permanent. Viral infections such as the MUMPS and bacterial EPIDIDYMITIS may damage or destroy testicular tissue. CHROMOSOMAL DISORDERS such as KLINEFELTER'S SYNDROME and endocrine disorders may affect TESTOSTERONE production. Congenital absence of the VAS DEFERENS, which often occurs in men who have CYSTIC FIBROSIS, prevents sperm from leaving the TESTICLES.

MALE INFERTILITY FACTORS

agricultural pesticide exposure	ATHEROSCLEROSIS
CHEMOTHERAPY	chronic ORCHITIS
chronic PROSTATITIS	chronic URETHRITIS
cigarette smoking	CRYPTORCHIDISM
CUSHING'S SYNDROME	CYSTIC FIBROSIS
DIABETES	DOWN SYNDROME
ERECTILE DYSFUNCTION	excessive ALCOHOL consumption
HYDROCELE	KLINEFELTER'S SYNDROME
HYPOGONADISM	low SPERM count
low SEMEN volume	malformed sperm
low sperm motility	prolonged elevated body temperature
OBESEITY	SICKLE CELL DISEASE
RADIATION THERAPY	substance abuse
RETROGRADE EJACULATION	testicular trauma
SPERMATOCELE	untreated HYPOSPADIAS
TESTICULAR CANCER	untreated HYPOSPADIAS
untreated EPISPADIAS	viral or bacterial EPIDIDYMITIS
VARICOCELE	

Combined factor infertility In combined factor infertility the reason for infertility results from the unique combination of factors each partner brings to the couple. A third of infertility circumstances arise from combined factors or remain unknown in their origin. Combined factors may be elements that, on their own, would not be sufficient to prevent conception. In particular combinations, however, these elements result in infertility. The woman's IMMUNE SYSTEM may generate antibodies that attack the man's sperm. Combined factor infertility is often the most difficult to sort out and treat.

Symptoms and Diagnostic Path

The primary symptom of infertility is the absence of pregnancy after one year of unprotected SEXUAL INTERCOURSE when pregnancy is the desired out-

come. The diagnostic path begins with comprehensive medical examination, including PELVIC EXAMINATION for women, and detailed history of attempts to conceive. Further diagnostic procedures depend on the preliminary findings and suspicions, though typically include laboratory tests for STDs, BLOOD tests for antibodies and HORMONE levels for the woman, and semen analysis for the man.

Additional diagnostic procedures for the woman may include

- basal body temperature journaling over several months to assess ovulation
- pelvic or transvaginal ULTRASOUND to examine the OVARIES and reproductive organs
- analysis of vaginal fluids to assess acidity (pH) and mucus
- hysterosalpingogram, a contrast medium X-RAY examination of the uterus and fallopian tubes
- karyotyping to detect chromosomal abnormalities such as TURNER'S SYNDROME
- exploratory laparoscopy to visually examine the internal pelvic structures

Additional diagnostic procedures for the man may include

- blood tests to measure hormone levels
- scrotal ultrasound to detect HYDROCELE, VARICOCELE, or SPERMATOCELE
- karyotyping to detect chromosomal abnormalities such as Klinefelter's syndrome

Treatment Options and Outlook

Treatment targets the identified or suspected cause. Basic approaches include frequent sexual intercourse, sexual positions that support conception, and timing sexual intercourse with ovulation. These basic measures result in conception within two years in about a third of couples. Other straightforward solutions may include treatment for infections or endocrine disorders (such as previously undiagnosed HYPOTHYROIDISM OR ADRENAL INSUFFICIENCY).

Further treatment is more invasive. In men, such treatment may consist of surgery to repair hydrocele, varicocele, or spermatocele. Testosterone supplementation often improves sperm

production and erectile function in men whose blood testosterone levels are low. In women, further treatment may include surgery to correct or repair various situations that contribute to or cause female factor infertility such as abdominal adhesions, ENDOMETRIOSIS, UTERINE FIBROIDS, certain uterine malformations, blocked fallopian tubes, and OVARIAN CYST. Hormone supplementation may regulate the MENSTRUAL CYCLE to encourage or stimulate ovulation ("superovulation") in women. Some hormones used in this way are off-label (not approved for infertility treatment though approved for other uses) in the United States.

Fertility experts select hormone therapies according to the underlying cause for ovulatory dysfunction, the woman's age, and any existing health conditions. Hormone treatment for infertility may have serious side effects, risks, and complications, including HOT FLASHES, mood swings, ovarian cyst formation, increased risk for spontaneous ABORTION early in pregnancy (miscarriage), and high risk for pregnancy with multiples (twins or greater). The long-term risks associated with fertility drugs, for the women who take them as well as the children conceived with their assistance, remain uncertain because the drugs have not been in use long enough to allow comprehensive studies.

MEDICATIONS USED TO STIMULATE OVULATION

bromocriptine

cabergoline

clomiphene citrate

FOLLICLE-STIMULATING HORMONE (FSH)

GONADOTROPIN-RELEASING HORMONE (GNRH) analogs

human chorionic gonadotropin (hCG)

human menopausal gonadotropin (hMG)

letrozole

metformin

ART methods to combine sperm and ova may be appropriate when there are no measures to correct the cause of infertility or attempted treatments have not succeeded.

Risk Factors and Preventive Measures

The primary risk factor for infertility is age. Though the time frame of fertility is clearly defined in women, fertility diminishes to some degree in men as they grow older. Lifestyle risk factors include cigarette smoking, alcohol consumption, environmental hazard exposure (such as pesticides), and obesity. Lifestyle also influences some health risks for infertility such as DIABETES, ATHEROSCLEROSIS, and infection with STDs. Risks for which there are no preventive measures include GENETIC DISORDERS and chromosomal disorders, CONGENITAL ANOMALY of the reproductive organs, POLYCYSTIC OVARY SYNDROME (PCOS), PREMATURE OVARIAN FAILURE (POF), endocrine disorders, and AUTOIMMUNE DISORDERS.

See also [ADOPTION](#); AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; [AMENORRHEA](#); BIRTH DEFECTS; FETAL ALCOHOL SYNDROME; [GENITAL TRAUMA](#); KARYOTYPE; OFF-LABEL USE; [PUBERTY](#); SMOKING AND HEALTH; SMOKING CESSATION; SURGERY BENEFIT AND RISK ASSESSMENT; [TUBAL LIGATION](#); [VASECTOMY](#).

intraductal papilloma A benign (noncancerous) tumor that grows within a lactiferous duct (milk duct) of a woman's BREAST. Intraductal papilloma is the most common cause of nipple discharge, which is its primary symptom. The discharge may be milky, clear, or blood tinged. A woman may notice only slight staining on her clothing. There is usually no PAIN or discomfort associated with intraductal papilloma.

The tumor causing symptoms may be too small for the woman or her health-care provider to feel, though may appear on MAMMOGRAM and usually shows up on ULTRASOUND of the breast. Other diagnostic procedures may include a contrast X-RAY called a ductogram and laboratory analysis of the nipple discharge. Biopsy of the papilloma, usually in combination with its surgical removal, provides definitive diagnosis. Intraductal papilloma occasionally recurs.

See also [BREAST CANCER](#); [BREAST HEALTH](#); [FIBROCYSTIC BREAST DISEASE](#).

K-L

Klinefelter's syndrome A chromosomal disorder affecting only males in which there is at least one extra X CHROMOSOME. The normal chromosomal configuration for a male is XY; the female configuration is XX. The extra X chromosome in a male, which doctors commonly designate as 47 XXY, dilutes the SECONDARY SEXUAL CHARACTERISTICS. Men who have Klinefelter's syndrome often do not produce SPERM and thus are infertile (unable to cause PREGNANCY).

Klinefelter's syndrome often does not become apparent until a boy enters (or fails to enter) PUBERTY. Secondary sexual characteristics are slow to develop and may appear effeminate, with small GENITALIA, enlarged breasts (GYNECOMASTIA), and little facial HAIR. LEARNING DISORDERS are also common in boys who have Klinefelter's syndrome, though researchers are uncertain of the reason for this. Adult men often experience SEXUAL DYSFUNCTION such as low LIBIDO, ERECTILE DYSFUNCTION, and INFERTILITY.

The diagnostic path includes BLOOD tests to measure the levels of TESTOSTERONE, LUTEINIZING HORMONE (LH), and FOLLICLE-STIMULATING HORMONE (FSH). Karyotyping, a representation of the chromosomal configuration of the cells, shows the extra X chromosome (and in some men, more than one extra X chromosome). Treatment is TESTOSTERONE supplementation to restore to normal the level of testosterone in the blood circulation. Testosterone supplementation generally results in increased masculinization (appearance of secondary sexual characteristics) such as thickened beard growth, deepened voice, enlarged PENIS and TESTICLES, and increased MUSCLE mass and definition. Treatment is generally lifelong.

See also CHROMOSOMAL DISORDERS; GENETIC DISORDERS; KARYOTYPE; TURNER'S SYNDROME.

letdown reflex The release of milk from the lactiferous glands and ducts to the nipple of the BREAST to initiate BREASTFEEDING (nursing). The first sucking motions the infant makes when attaching to the nipple are rapid and pulling. These motions stimulate the release of OXYTOCIN from the PITUITARY GLAND, which causes the tissues around the ducts to contract to push the milk to the nipple. The mother feels this release and the initial flow of milk as a tingling sensation. The more full of milk the breasts are the more intense the sensation. Letdown occurs multiple times during a breastfeeding session. Other events may also stimulate the letdown REFLEX, such as the sound of the infant's cry. Letdown affects both breasts, often causing milk to leak from the un-nursed breast.

See also PREGNANCY.

libido The level of sexual desire an individual feels, also called sex drive. Libido represents a complex interaction between the mind and the sex hormones. Low hormonal levels often result in reduced libido. In men the HORMONE associated with libido is TESTOSTERONE; in women both ESTROGENS and testosterone play roles in libido. Numerous medications, serious or chronic illness, long-term ALCOHOLISM, and substance abuse may also reduce libido. As well, libido typically slows with age.

Indications or symptoms of low libido may include

- lack of interest in sex
- lack of sexual arousal
- inability to reach ORGASM
- ERECTILE DYSFUNCTION in men
- reduced vaginal lubrication in women

Hormone supplementation often improves libido when hormone levels are the cause for its decline. Treating health conditions that may cause low libido, or changing medications that can affect libido, is sometimes all the treatment that is neces-

sary. Libido also often has significant emotional and psychologic components. Treatment for low libido depends on its identifiable causes.

See also [SEXUAL DYSFUNCTION](#); [SEXUAL HEALTH](#); [SEXUAL INTERCOURSE](#).



mammogram An X-RAY examination of the BREAST. The most common use of mammogram is for early detection of BREAST CANCER. However, mammogram may be a diagnostic tool in the evaluation of various conditions that affect the breasts. Most abnormal findings mammograms detect are not cancer.

Most often a woman stands for a mammogram. The technologist places one breast on a shelf on the X-ray machine, beneath which is the X-ray film. A moving shelf then compresses the breast against the shelf to somewhat flatten the breast tissue for better visualization. With routine screening mammogram the technologist takes two X-rays of each breast, one from the side and one from above. The entire procedure—positioning and taking the images—takes about 10 minutes. With diagnostic mammogram the technologist takes up to five images, in different positions, of each breast. The entire procedure for diagnostic mammogram takes about 15 minutes.

Though mammogram is generally quick and painless, some women experience discomfort with the compression of their breasts. Women who are still menstruating should have routine mammograms two weeks after the end of their menstrual periods to minimize discomfort, as the breasts are least sensitive at this time.

Most health-care providers recommend routine screening mammograms beginning at age 40 for women who have no unusual risks for breast cancer—every two years between ages 40 and 50 and once a year after age 50. Women who have had breast cancer or have three or more risk factors for breast cancer should talk with their doctors about the appropriate intervals for mammogram. Because the breast tissue of menstruating women is very dense it blocks visualization of abnormali-

ties, making screening mammogram impractical in younger women. With MENOPAUSE the breast tissue becomes considerably less fatty and dense, so abnormal growths are readily obvious. Mammogram often can detect growths and tumors in the breast before they reach a size at which the woman or her health-care provider can feel them.

See also [BREAST SELF-EXAMINATION](#); [CANCER PREVENTION](#); [FIBROCYSTIC BREAST DISEASE](#); [PREVENTIVE HEALTH CARE AND IMMUNIZATIONS](#).

mastalgia Painful breasts. Cyclic mastalgia in women occurs commonly with MENSTRUATION. Noncyclic mastalgia in women may indicate MASTITIS (INFLAMMATION, often the result of bacterial INFECTION). Mastalgia in women is also common during PREGNANCY and BREASTFEEDING. Mastalgia is uncommon in men and signals an underlying condition that requires a doctor's evaluation.

Mastalgia is a symptom rather than itself a health condition. The diagnostic path attempts to pinpoint the cause of the PAIN. Diagnostic procedures the doctor may conduct include breast ULTRASOUND and MAMMOGRAM (X-RAY of the BREAST). Treatment targets the underlying cause.

See also [GYNECOMASTIA](#).

mastectomy A SURGICAL OPERATION to remove the BREAST. Mastectomy is most commonly a treatment for BREAST CANCER. Women who have extraordinarily high risk for breast cancer (such as because of family history or known MUTATION of the BRCA-1/BRCA-2 genes) may choose prophylactic mastectomy, also called risk-reduction mastectomy, to reduce the likelihood that they will develop cancer. Mastectomy is a major surgery that may require two to five days of hospitalization after the operation, depending on the extent

of the surgery. Women may choose to have immediate or follow-up breast reconstructive surgery, or no reconstruction.

Surgical Procedure

A woman undergoing mastectomy receives general ANESTHESIA. The operation generally takes two to four hours; mastectomy with reconstruction takes longer than mastectomy alone. There are three types of mastectomy:

- Segmental mastectomy is when the surgeon removes the tumor and the quadrant of breast that contains it. The surgeon may recommend this operation when the breast cancer tumor is small and localized though larger than would be appropriate for lumpectomy (removal of the tumor and a margin of the surrounding breast tissue).
- Subcutaneous mastectomy, also called SKIN-sparing mastectomy, is removal of the breast tissue with the nipple, areola, and surface skin of the breast remaining. Subcutaneous mastectomy affords the most ideal circumstance for breast reconstruction.
- Total mastectomy, also called simple mastectomy, removes all of the breast tissue including the nipple and areola. The surgeon may recommend total mastectomy when the cancer is diffuse (lacking clear boundaries) or in more than one location within the breast. The surgeon may also perform SENTINEL LYMPH NODE DISSECTION, a method that examines the first LYMPH NODE in the drainage path from the tumor. Whether the sentinel contains cancer cells is an accurate indicator of whether the cancer has spread from the breast.
- Modified radical mastectomy removes all of the breast, including the nipple and areola, as well as the axillary LYMPH nodes (lymph nodes under the arm), called axillary lymph node dissection. This is the operation of choice when the cancer tumor is fairly large or diagnostic scans show the lymph nodes contain cancer.

After removing the breast the surgeon places small tubes to drain fluid from the surgical site during the initial stages of HEALING and then sutures closed the surgical incision. The surgeon

removes the drains three to seven days after the operation, usually before the woman leaves the hospital. The nature and extent of scarring and deformity depends on the type of mastectomy. If there are skin sutures, they are usually ready for removal in five to seven days.

Risks and Complications

As with any surgery, the risks of mastectomy include excessive bleeding, INFECTION, and reaction to the anesthesia. These risks are slight. The potential for complications increases with the complexity of the surgery. Women who undergo modified radical mastectomy with axillary lymph node dissection may have significant swelling in the arm on the side of the surgery in the immediate postoperative recovery period as well as intermittently over the long term. Many women undergo adjuvant therapy (follow-up treatment), such as RADIATION THERAPY OR CHEMOTHERAPY, after mastectomy for breast cancer. These therapies carry their own risks and do not usually affect the course of healing from the surgery.

Outlook and Lifestyle Modifications

With early detection and treatment, recovery from both the mastectomy and the breast cancer is complete. Recovery from modified radical mastectomy can take several months, with restrictions on lifting and some physical activities until the area fully heals and swelling (LYMPHEDEMA) is under control. It is difficult to predict who will have ongoing lymphedema; this is a significant long-term risk for any woman whose surgery includes axillary lymph node dissection. Women who choose not to have reconstructive surgery may opt instead for prosthetic bras. Many women have concerns about body image and sexuality; these are potentially significant issues that can affect QUALITY OF LIFE. Some women find SUPPORT GROUPS helpful.

See also CANCER TREATMENT OPTIONS AND DECISIONS; HORMONE-DRIVEN CANCERS; PAGET'S DISEASE OF THE BREAST; PLASTIC SURGERY; SURGERY BENEFIT AND RISK ASSESSMENT.

mastitis INFLAMMATION of the BREAST, typically due to bacterial INFECTION. Mastitis usually begins as a combination of events: a blocked milk duct in

the breast of a woman who is BREASTFEEDING an infant and cracks or breaks in the SKIN, usually around the nipple, that allow BACTERIA to enter the milk duct. Mastitis due to infection is less common in women who are not breastfeeding. Mastitis may also occur as a result of viral infection or become chronic for reasons the doctor cannot identify though are likely hormonal.

Bacterial Mastitis

The symptoms of bacterial mastitis include PAIN, redness on the skin above the area of the infection, and swelling or hardness at the site of the infection. Many women also have FEVER, chills, bodywide MUSCLE aches, and fatigue. It is important for breastfeeding women to continue breastfeeding, as the infant's sucking helps massage the blockage from the duct. Warm compresses or a heating pad to the breast also may help.

A course of treatment with an antibiotic medication generally results in rapid improvement of bacterial mastitis. The small amount of the antibiotic that enters the breast milk is not enough to affect the infant. The doctor may recommend an analgesic medication to relieve pain and fever. A complication of bacterial mastitis is breast ABSCESS, in which the infection forms a pocket within the breast tissue that requires minor surgery to open and drain, as well as a more extended course of antibiotics, so HEALING can take place.

**ANTIBIOTIC MEDICATIONS
TO TREAT BACTERIAL MASTITIS**

amoxicillin-clavulanic acid	cephalexin
ciprofloxacin	clindamycin
cloxacillin	flucloxacillin

Nonbacterial Mastitis

Mastitis may also result from viral infection, most commonly as a result of the MUMPS VIRUS. Nonspecific chronic mastitis sometimes occurs in a pattern that follows a woman's MENSTRUAL CYCLE, suggesting it is hormonal in nature. The diagnostic path for nonbacterial mastitis often includes MAMMOGRAM (X-RAY of the breasts) and sometimes biopsy of an area of inflammation to rule out BREAST CANCER or other causes for the symptoms. When such findings are negative, treatment is generally NONSTEROIDAL ANTI-INFLAMMATORY DRUGS

(NSAIDS) to relieve inflammation and pain. NSAIDs also influence the production and release of PROSTAGLANDINS, hormonelike substances that fluctuate in the BLOOD circulation during the menstrual cycle. Chronic mastitis is a common symptom of FIBROCYSTIC BREAST DISEASE.

See also ANALGESIC MEDICATIONS; ANTIBIOTIC MEDICATIONS; [HORMONE](#); [MASTALGIA](#).

masturbation Touching one's own body, and in particular the genitals, for sexual pleasure and typically to reach ORGASM. Masturbation is a normal behavior most common among adolescents and young adults. Masturbation does not cause adverse health effects, either of the genitals or health in general. For several centuries myths have persisted that masturbation causes blindness, mental illness or insanity, HAIR growth on the palms of the hands, INFERTILITY, and other problems. These myths arise from social and cultural attitudes toward masturbation, not from medical science. Excessive masturbation may indicate underlying psychologic or emotional conditions. Inappropriate masturbation (notably public masturbation) is often an indication of serious mental illness, DEMENTIA, or BRAIN damage (such as due to STROKE or trauma), conditions that disturb the normal inhibitory mechanisms of conscious behavior.

See also [SEXUAL DYSFUNCTION](#); [SEXUAL INTERCOURSE](#).

menarche A woman's first menstrual period, the start of MENSTRUATION and the beginning of FERTILITY. The average age of menarche varies among cultures and countries throughout the world and largely correlates with nutritional well-being. In the United States the average age of menarche is 12½; in rural regions of South Africa the average age of menarche is near age 14. The age of menarche has declined worldwide by nearly a year over the past century, which health experts believe reflects improved nutrition and overall health status. Many cultures celebrate menarche as a rite of passage that ushers a girl into womanhood.

See also [AMENORRHEA](#); [MENOPAUSE](#); [MENSTRUAL CYCLE](#).

menopause A woman's last menstrual period, the end of MENSTRUATION and the closure of a

woman's FERTILITY. Though researchers understand the cascade of physiologic events that results in menopause, the triggering factors remain a mystery though many researchers believe a key triggering mechanism is the loss of viable eggs (ova). Doctors consider a woman to have reached menopause when she has experienced one continuous year (12 contiguous months) without menstrual periods. However, the common perception of menopause encompasses the period of time, often years, preceding menopause. Some people call this time PERIMENOPAUSE ("around menopause").

Though menopause is a natural life shift, not a health condition or disorder, many women experience discomforts as their bodies rebalance after HORMONE levels shift. Most notable among these discomforts are HOT FLASHES, irregular menstrual periods or abnormal vaginal bleeding, and mood changes. Not all women experience all or even any of these discomforts; some women experience additional or different discomforts such as joint pain and HEADACHE. The transition of menopause is a uniquely individual passage.

Indications of Menopause

The most defining indication of menopause is the discontinuation of menstruation. In most women this occurs as a gradual process during which menstrual periods become increasingly irregular both in timing and quality. A woman may have three periods that are three weeks apart and last eight or nine days each, have one three-day period six weeks later, then not have another period for four months. This pattern may extend over three to five years, during which a woman typically experiences other indications that her hormone levels are fluctuating and dropping. Such indications commonly include

- vaginal dryness and painful sexual intercourse
- hot flashes and night sweats
- tendency to cry, mood swings, and irritability
- difficulty sleeping
- diminished ability to concentrate and memory difficulties
- decreased LIBIDO (sex drive)
- anxiety or DEPRESSION

Some women barely notice any of these indications and other women find that they interfere with nearly all aspects of their lives. There are few clinical answers to explain the broad range of experience, nor to predict what course a particular woman's menopause experience will take. There is some indication that a woman tends to have an experience similar to her mother's, though whether the reasons are cultural or physiologic remains unknown.

Relieving Menopause Discomforts

There are numerous approaches to relieving the discomforts of menopause, some of which are clinical and others that are alternative and lifestyle. The more a woman understands the changes that are occurring in her body and the natural course they represent, the more effectively she can cope with their effects and choose methods of relief that are appropriate for her health status and her degree of discomfort. Many women find the most effective solutions involve a mix of methods, and that the mix changes as menopause progresses.

Hormone replacement therapy (HRT) For the last half of the 20th century doctors treated menopause with hormone replacement therapy (HRT), hormone supplementation to elevate the levels of ESTROGENS and PROGESTERONE in the BLOOD circulation. The intent of HRT was to bring up these levels enough to relieve discomforts without restoring the menstrual cycle. Doctors also believed HRT helped protect a woman from CARDIOVASCULAR DISEASE (CVD) and OSTEOPOROSIS, two conditions that can have dire consequences as a woman ages. The foundation for this belief was the sharp rise in incidence of HEART ATTACK and the high rate of osteoporosis among women after menopause who did not take HRT. It seemed that women who took HRT were less likely to have either condition. Many American women took HRT for the last half of their lives.

However, extensive clinical studies began to show in the early 2000s that contrary to these popular perceptions, HRT did not have a protective effect against CVD and had perhaps a limited protective benefit for osteoporosis. Further, HRT significantly increased the risk for some types of HORMONE-DRIVEN CANCERS, such as BREAST CANCER and ENDOMETRIAL CANCER. In 2002 health agencies

withdrew recommendations for routine long-term HRT, advising that doctors instead prescribe time-limited hormone supplementation to relieve menopausal discomforts only when they interfered with a woman's QUALITY OF LIFE. Under the current standard of practice guidelines most women should not take hormone supplementation for longer than two years, with a trial off the supplementation every six months to assess whether it remains necessary. Each woman's individual health circumstances require her doctor's careful evaluation to determine whether hormone supplementation is appropriate.

There is a sizable group of health-care professionals who prescribe BIHRT (bio-identical hormone replacement therapy). BIHRT utilizes hormones such as estradiol, progesterone, and testosterone that are chemically identical to those found in the woman's body. It is felt by many that not only do they not pose the same health risks as were identified in the WHI study but do actually provide numerous health benefits.

Nonhormonal approaches Selective serotonin reuptake inhibitors (SSRIs), a class of ANTIDEPRESSANT MEDICATIONS, have emerged as effective therapies to relieve hot flashes. Doctors usually prescribe these medications at doses lower than those typically used to treat depression. Researchers do not know the precise mechanisms through which SSRIs relieve hot flashes.

There are numerous alternative or complementary approaches to relieve menopausal discomforts, some of which show evidence of their success through clinical studies. Among them include ACUPUNCTURE, SOY, and the medicinal herb BLACK COHOSH, all to relieve hot flashes, and wild yam cream to relieve vaginal dryness. Soy and black cohosh contain PHYTOESTROGENS, plant-based substances that are similar to human estrogens and bind with estrogen receptors in the body, though with less intensity than endogenous estrogens. Wild yams contain a plant-based form of progesterone.

Other remedies are widely believed to provide relief but lack evidence, either because studies have not been done or have produced inconclusive or conflicting results. Among these are black cohosh to relieve mood swings and irritability and DONG QUAI, soy, and red clover to relieve hot

flashes and other discomforts. Evening primrose oil and vitamin E supplements appear to help with relaxation and sleep.

ALTERNATIVE REMEDIES TO TREAT MENOPAUSAL DISCOMFORTS	
ACUPUNCTURE	BLACK COHOSH
DONG QUAI	evening primrose oil
red clover	SOY
vitamin E	progesterone cream

Changes That Occur with Menopause

Estrogen has multiple and powerful actions in a woman's body and the decline of its presence after menopause results in changes that affect all body systems. One such action is a diminished ability to repair collagen structures in the body such as ligaments, tendons, and the SKIN. The loss of collagen may affect the ligaments in the abdomen that support the UTERUS, particularly in women who have given birth, resulting in UTERINE PROLAPSE. A good number of women experience URINARY INCONTINENCE as a result of weakening of the muscles that control the flow of URINE; KEGEL EXERCISES often improve or prevent this. The skin thins and becomes less elastic, resulting in wrinkles. Sebaceous secretions also diminish, causing the skin to become dry. The mucous lining of the VAGINA thins as well, resulting in reduced vaginal secretions. The more fragile vagina may produce symptoms such as burning and itching (VAGINITIS) and discomfort during SEXUAL INTERCOURSE.

Changes in collagen also affect the walls of the arteries, causing them to become less flexible and less able to relax (dilate). As well, estrogen plays a key role in the METABOLISM of cholesterol and fatty acids. As estrogen levels drop the body handles these lipids less efficiently. Consequently HYPERLIPIDEMIA, ATHEROSCLEROSIS, and HYPERTENSION (high BLOOD PRESSURE) become more common after menopause. In addition, loss of estrogen (specifically estradiol) can contribute to HYPOTHYROIDISM and increased CORTISOL potentially leading to INSULIN RESISTANCE. Estrogen also acts as a natural selective serotonin reuptake inhibitor (SSRI) so its loss contributes to increased DEPRESSION. Nutritious EATING HABITS and daily physical exercise become especially important to maintain cardiovascular health in light of these changes.

Estrogen is also essential for maintaining the content of calcium and other bone-building minerals. After menopause calcium more easily leaves the bones and is less easily absorbed into the blood circulation from dietary sources, a double effect that can rapidly result in osteoporosis. More than two thirds of women over age 65 have some degree of osteoporosis. Calcium supplementation in combination with RESISTANCE EXERCISE (also called weight-bearing exercise) helps the bones to retain the calcium they require to remain dense and strong.

See also AMENORRHEA; BONE; BONE DENSITY; CHOLESTEROL, ENDOGENOUS; EXERCISE AND HEALTH; GENERAL ANXIETY DISORDER (GAD); HYSTERECTOMY; MEDICINAL HERBS AND BOTANICALS; MENARCHE; PREMATURE OVARIAN FAILURE (POF).

menstrual cramps See DYSMENORRHEA.

menstrual cycle The pattern of hormonal and physiologic changes that occur that occur in a woman's body in preparation for possible PREGNANCY. Though the average menstrual cycle spans 28 days, the frequency of MENSTRUATION varies widely among women and often within each woman individually. Menstrual cycles may be as short as 25 days or as long as 32 days and still be within the range of normal. Menstrual cycles outside these parameters may or may not be normal, depending on the woman's individual physiology and health status. The endocrine system directs the menstrual cycle.

Physiologic Phases of the Menstrual Cycle

There are four phases within the menstrual cycle that always occur in the same order:

1. The proliferative phase begins with the end of menstruation and the return of the endometrium (lining of the UTERUS) to its non-menstrual state and culminates with OVULATION about 14 days after the onset of menstruation. During proliferation the level of ESTROGENS in the BLOOD circulation rises and the level of PROGESTERONE drops. The changing hormone levels stimulate the maturation of up to 20 ova within their ovarian follicles, called ripening. The follicle containing the first ovum to reach full maturity ruptures and releases the ovum into the fluid surrounding the fimbriae (fluted edges) of the fallopian tube. The other follicles that had started to develop then shrink; the ovary absorbs them and their ova.
2. The expelled ovum leaves behind the corpus luteum, a structure of endocrine tissue that begins secreting estrogens and progesterone. This period of activity by the corpus luteum is the luteal phase, also called the secretory phase. The increased blood levels of the hormones cause the endometrium to thicken and its blood vessels to enlarge. The glands that line the endometrium increase their secretions, and the inner endometrium becomes spongy and engorged in preparation to support implantation should CONCEPTION occur. The luteal phase lasts about 10 days.
3. When the ovum passes through the uterus without implanting, the corpus luteum involutes (turns in on itself) and the follicle absorbs it. The sudden drop in estrogens and progesterone causes the endometrial blood vessels to contract, called endometrial ischemia. The endometrial glands stop their secretions and the endometrium dramatically shrinks. This third phase of the menstrual cycle, called the ischemic phase, lasts 36 to 48 hours.
4. The culminating phase of the menstrual cycle is menstruation, during which the anemic (blood-deprived) tissue of the endometrium sloughs away and passes from the body. The menstrual flow contains tissue fragments, endometrial secretions, and blood. Menstruation lasts 3 to 5 days in 85 percent of women; about 15 percent of women menstruate for 7 days. Though menstruation is the last phase of the menstrual cycle, doctors consider the first day of menstrual bleeding to be the start of the menstrual cycle.

Endocrine Regulation of the Menstrual Cycle

The HYPOTHALAMUS, PITUITARY GLAND, and corpus luteum regulate the menstrual cycle. The hypothalamus initiates the proliferative phase of the menstrual cycle by releasing GONADOTROPIN-RELEASING HORMONE (GNRH). GnRH stimulates the pituitary gland to secrete a surge of FOLLICLE-STIMULATING

HORMONE (FSH), which induces an ovarian follicle to begin secreting estrogens. The estrogens cause the ovum within the follicle to begin ripening. The rising level of estrogens in the blood circulation triggers the hypothalamus to again release GnRH, which this time stimulates the pituitary gland to secrete LUTEINIZING HORMONE (LH). LH causes the ovarian follicle to produce progesterone, which brings the ovum to maturity and release (ovulation). Without pregnancy the blood levels of estrogens and progesterone both fall and menstruation takes place.

Disturbances of the Menstrual Cycle

Numerous factors may disrupt the menstrual cycle, the most common being pregnancy. When a fertilized ovum (ZYGOTE) implants in the endometrium, the menstrual cycle ends and pregnancy begins. The menstrual cycle does not return until six to eight weeks (and sometimes longer, up to months in women who are breastfeeding) after CHILDBIRTH. Hormonal imbalances may also disrupt the menstrual cycle. HYPOTHYROIDISM (underactive thyroid gland) or HYPERTHYROIDISM (overactive thyroid gland) is a common source of such hormonal disruption. Disorders of the pituitary gland, such as pituitary ADENOMA, or the ADRENAL GLANDS, such as ADRENAL INSUFFICIENCY, often alter the body's endocrine matrix in ways that affect the menstrual cycle.

Numerous medications and treatments such as CHEMOTHERAPY and RADIATION THERAPY may affect ovarian function. Menstrual disturbances may occur as a result of underlying health conditions such as POLYCYSTIC OVARY SYNDROME (PCOS), OBESITY, anorexia, and extreme emotional or physical stress. Though a normal menstrual cycle often occurs with a single functioning ovary, the absence or loss of both OVARIES ends the menstrual cycle. OOPHORECTOMY is the surgical OPERATION to remove an ovary. Women who participate in intense athletic activities, such as marathons and triathlons, may have irregular menstrual cycles or AMENORRHEA (absence of menstruation).

For further discussion of the menstrual cycle within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System." For further discussion of the menstrual cycle within

the context of the structures and functions of the endocrine system, please see the overview section "The Endocrine System."

See also [DYSFUNCTIONAL UTERINE BLEEDING \(DUB\)](#); [DYSMENORRHEA](#); [FALLOPIAN TUBES](#); [FERTILITY](#); [INFERTILITY](#); [MENARCHE](#); [MENOPAUSE](#); [PREMATURE OVARIAN FAILURE \(POF\)](#); [PREMENSTRUAL SYNDROME \(PMS\)](#).

menstruation The final phase of the MENSTRUAL CYCLE, commonly called the menstrual period or simply the period. Menstruation is the discharge of BLOOD and excess tissue that build up within the UTERUS as endometrium (the lining of the uterus) thickens and engorges with blood in preparation for the implantation of a fertilized ovum (ZYGOTE). When PREGNANCY does not occur, hormonal changes cause the lining to slough away, passing from the uterus and out of the body via the VAGINA. Typically a woman passes two to three ounces of blood and other fluids over the course of the three to seven days she menstruates. The menstrual flow is generally heaviest on the second through the fourth days. About 85 percent of women menstruate for four to five days; about 15 percent menstruate for six to seven days.

Women typically use disposable sanitary napkins (commonly called pads) or tampons to capture the menstrual flow. Pads have adhesive strips that attach them to underwear; tampons fit inside the vagina. It is important to change either pads or tampons every four to six hours to prevent overflow and maintain appropriate PERSONAL HYGIENE. Tampons may irritate the vaginal walls. Because a tampon may carry BACTERIA into the vagina when the woman inserts, tampon use involves a slight risk for TOXIC SHOCK SYNDROME, a potentially life-threatening INFECTION. Doctors recommend using pads at night and during other times when it might not be possible or practical for a woman to change her sanitary protection every four to six hours.

There are no health reasons for women to avoid their regular activities, including sports, bathing, and sexual activity if desired, during menstruation. Women may prefer to shower when menstruating. Washing the GENITALIA with gentle soap and warm water is important to cleanse any accumulated menstrual fluids from the genital tissues, which reduces the presence of

bacteria as well as improves comfort. Many women wear tampons during athletic activities such as bicycling, swimming, dancing, and running. However, a woman should not sit in the bath tub or in a hot tub while wearing a tampon because the combination of heat and inactivity may draw bacteria into the vagina via the tampon's removal cord, which extends from the vaginal opening. A woman should also change her tampon immediately after water activities such as swimming.

For further discussion of menstruation within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; AMENORRHEA; DYSMENORRHEA; MENARCHE; MENOPAUSE; OVA; PUBERTY.

miscarriage See ABORTION.

mittelschmerz Discomfort a woman may feel on one side of her lower abdomen around the time she ovulates. The word is German for "middle pain," a reference to the occurrence of the discomfort midway through the MENSTRUAL CYCLE. The discomfort is often a sharp, achy pain that most commonly lasts from 2 to 12 hours though may continue up to 48 hours. Some women find the discomfort shifts sides from one menstrual period to another and some women have discomfort always on the same side. The side of the pain does not necessarily indicate which ovary is releasing an ovum as ovarian pain may refer to the opposite side of the lower abdomen.

Doctors believe mittelschmerz results from irritation the released ovum and the fluids that surround it create in the abdominal cavity, or from the pressure of the ovarian follicle immediately before its rupture to release the ovum. Mittelschmerz is a normal part of the menstrual cycle for many women and does not signal any underlying health concerns, though a doctor should evaluate any changes that may occur in the nature of the discomfort.

See also OVA; OVARIAN CYST; OVULATION.

morning sickness The NAUSEA and VOMITING that may occur during PREGNANCY, notably in the first

trimester though it may continue through the second trimester and occasionally for the duration of the pregnancy. The term morning sickness is a misnomer as the nausea may occur at any time, day or night. However, many women do experience the nausea of pregnancy primarily in the morning when they first awaken. Many women find certain odors, tastes, or even appearances of food act as triggers for morning sickness.

Though doctors do not know for certain what causes morning sickness, they believe it is a reaction to the multitude of hormonal changes rapidly taking place in the woman's body as the pregnancy establishes itself. The onset of morning sickness, typically at about six weeks into the pregnancy, correlates with the surge of human chorionic gonadotropin (hCG) that emerges from the newly formed PLACENTA. Morning sickness, though disruptive, is not harmful for the pregnancy unless it prevents the woman from drinking enough water to remain hydrated. Most weight gain in pregnancy occurs in the second and early part of the third trimesters, and most women are able to eat enough to remain well nourished.

Nonpharmaceutical remedies for morning sickness include

- gingerroot shavings or tea
- flat GINGER ale (made with real ginger)
- cola syrup (available in drugstores) or flat cola soda
- soda crackers (such as saltines)
- not mixing solids and liquids
- small meals eaten frequently throughout the waking hours, and small snacks when awake during the night, so there is always something in the STOMACH
- ACUPUNCTURE or acupressure (including motion sickness wristbands that apply pressure to acupuncture points for nausea)

If these efforts are unsuccessful and morning sickness interferes with normal eating and drinking, the doctor may recommend or prescribe ANTIEMETIC MEDICATIONS that are safe to take during pregnancy. Some women experience relief with vitamin B₆ supplement, though doctors are unsure why this is. Because some medications may be

harmful to, or have unknown effects on, the developing FETUS, it is important to talk with the doctor before taking any medication or herbal remedy.

The doctor may consider intravenous fluids and nutrition for women who experience severe, extended morning sickness (called hyperemesis gravidarum), though the need for such intervention is uncommon. Morning sickness is more common in women who have a history of migraine HEADACHE, motion sickness, or morning sickness in previous pregnancies. Morning sickness is also more common in women who are pregnant with multiples (twins or higher).

See also [PRENATAL CARE](#); VITAMINS AND HEALTH.

nabothian cyst A mucous-filled growth that develops within a nabothian gland. The nabothian glands are clusters of mucous-secreting cells on the surface of the CERVIX. Nabothian cysts are very common, cause no symptoms, and present no health risk. Typically the health-care provider discovers nabothian cysts, which are hard and pimplelike, during routine PELVIC EXAMINATION. Occasionally the doctor may choose to further examine nabothian cysts using COLPOSCOPY to confirm the diagnosis.

See also [BARTHOLIN'S CYST](#); [PAP TEST](#).

neonatal jaundice A condition in which the newborn infant's LIVER cannot yet properly destroy old erythrocytes (red BLOOD cells), resulting in the accumulation of BILIRUBIN in the blood circulation. The excessive bilirubin, a pigmented protein com-

pound, gives the SKIN a characteristic yellowish orange hue. Neonatal JAUNDICE, also called physiologic jaundice of the newborn, is more common in infants born before 37 weeks gestational age because of the immaturity of their livers.

Mild neonatal jaundice clears on its own within a few days. The doctor may prescribe photolight therapy (also called PHOTOTHERAPY) for moderate neonatal jaundice, a treatment that exposes the infant's skin to short periods of ultraviolet light. Ultraviolet light expedites the chemical breakdown of the bilirubin so the body can excrete it.

Circumstances of jaundice in a newborn may result from numerous pathologic causes including BILIARY ATRESIA (absence of the BILE DUCTS), BOWEL ATRESIA (absence of the large intestine), hemolytic disease of the newborn (Rh incompatibility), and congenital HEPATITIS B.

See also ANEMIA; BLOOD TYPE; ERYTHROCYTE.

nocturnal emission ORGASM and EJACULATION that occur when a boy or man is asleep. Nocturnal emissions are natural and normal across the age spectrum from ADOLESCENCE through old age, though are most common during adolescence when SECONDARY SEXUAL CHARACTERISTICS are developing and HORMONE levels are rising. Researchers believe nocturnal emissions often occur during dreams (thus the casual term "wet dreams") though the man may not remember dreaming.

See also AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; [MASTURBATION](#); [PUBERTY](#); [SEXUAL HEALTH](#).



oophorectomy A surgical OPERATION to remove one ovary (unilateral oophorectomy) or both OVARIES (bilateral oophorectomy) in a woman. Oophorectomy may be therapeutic (to treat a health condition) or prophylactic (to prevent a health condition).

The key health conditions for which therapeutic oophorectomy is an option include OVARIAN CANCER, severe ENDOMETRIOSIS, ovarian ABSCESS (INFECTION of the ovary), and large or multiple ovarian cysts. Prophylactic oophorectomy is an effort to lower the possibility for developing HORMONE-DRIVEN CANCERS (ovarian, breast, endometrial) in a woman who has unusually high risk for such cancers, either genetically or because of a prior such cancer. Removing both ovaries cuts a woman's estrogen production to almost nothing, mostly depriving hormone-sensitive cancer cells of the substance they require to thrive.

Unilateral oophorectomy often allows a woman to preserve her FERTILITY because the remaining ovary, if healthy, continues to produce hormones and OVA (eggs) that maintain the MENSTRUAL CYCLE. Bilateral oophorectomy entirely ends ovarian function and the menstrual cycle, resulting in abrupt MENOPAUSE in women who are still menstruating at the time of surgery. Such surgically induced menopause, because it is sudden, may thrust the body into significant symptoms such as HOT FLASHES.

The operation for either unilateral or bilateral oophorectomy may be OPEN SURGERY, in which the surgeon makes an incision in the lower abdomen large enough to expose the ovary, or MINIMALLY INVASIVE SURGERY, in which the surgeon makes several small incisions in the lower abdomen and visualizes the operative site using a laparoscope. The type of operation depends on multiple factors

including the reason for the oophorectomy and the woman's general health status. Open oophorectomy requires three to five days of hospitalization and six to eight weeks for recovery. Laparoscopic oophorectomy is often an ambulatory (outpatient) surgery with rapid recovery and return to regular activities within a week or two. About half of total hysterectomies (operations to remove the UTERUS) also include removal of the ovaries (hystero-oophorectomy) or the ovaries and the FALLOPIAN TUBES (hysterosalpingo-oophorectomy).

The short-term risks of oophorectomy include excessive bleeding and postoperative infection. The key long-term complication of bilateral oophorectomy is OSTEOPOROSIS (loss of BONE DENSITY), the risk for which arises from the depletion of estrogen.

See also BRCA-1/BRCA-2; [BREAST CANCER](#); CANCER TREATMENT OPTIONS AND DECISIONS; CA-125; [ENDOMETRIAL CANCER](#); [HYSTERECTOMY](#); LASER SURGERY; MINIMALLY INVASIVE SURGERY; [ORCHIECTOMY](#); [OVARIAN CYST](#); SURGERY BENEFIT AND RISK ASSESSMENT.

orchiectomy A surgical OPERATION to remove one testicle (unilateral orchiectomy) or both TESTICLES (bilateral orchiectomy) in a man. Unilateral orchiectomy is typically a treatment for TESTICULAR CANCER or severe TESTICULAR TORSION in which the testicle becomes gangrenous due to prolonged loss of BLOOD circulation. Bilateral orchiectomy is typically a treatment for advanced PROSTATE CANCER.

The testicles produce both TESTOSTERONE and SPERM. Many men who undergo unilateral orchiectomy retain their FERTILITY and full sexual function. However, other treatment such as CHEMOTHERAPY may affect sperm production and thus fertility. Bilateral orchiectomy ends produc-

tion of both testosterone and sperm, resulting in permanent INFERTILITY. The intent of bilateral orchiectomy is to cut the supply of testosterone that feeds prostate cancer cells, as prostate cancer is one of the HORMONE-DRIVEN CANCERS. The resulting precipitous decline in testosterone production often also diminishes LIBIDO (sex drive) and may cause ERECTILE DYSFUNCTION (difficulty achieving or sustaining an ERECTION).

For unilateral orchiectomy the surgeon removes the testicle through an incision in the lower abdomen, just above the pubic HAIR line. The incision exposes the inguinal canal, a passage of ligaments through which the testicles originally descended into the SCROTUM. The surgeon manipulates the testicle upward from the scrotum into the lower abdomen, extracting it through the incision. This procedure prevents damage to the scrotum that could allow cancer cells to escape into the LYMPH nodes; the testicles and the scrotum use different lymph networks so the surgeon does not want to disturb the scrotum or create a circumstance in which cells from the testicle can enter the lymph nodes that serve the scrotum. For bilateral orchiectomy as prophylactic treatment for advanced prostate cancer the surgeon may make the incision in the scrotum.

The key risks of orchiectomy include excessive bleeding and INFECTION. Unilateral orchiectomy sometimes lowers testosterone levels, which the doctor may treat with testosterone supplementation. Long-term complications that occur with bilateral orchiectomy include loss of BONE DENSITY and increased risk for OSTEOPOROSIS, GYNECOMASTIA (enlarged breasts), and erectile dysfunction.

See also GANGRENE; OOPHORECTOMY; ORCHIOPEXY; SURGERY BENEFIT AND RISK ASSESSMENT.

orchiopexy A surgical OPERATION to correct an undescended testicle (CRYPTORCHIDISM). Nearly always the operation takes place early in childhood, typically between ages six and 12 months. In many situations the operation is an outpatient procedure the surgeon can perform in an AMBULATORY SURGICAL FACILITY, usually with general ANESTHESIA.

The surgeon makes two incisions, one in the lower abdomen and one in the SCROTUM. The abdominal incision provides access to the unde-

scended testicle, which the surgeon manipulates through the inguinal canal (a passageway through the ligaments supporting the pelvic floor) and into the scrotum. Through the incision in the scrotum the surgeon sutures (stitches) the testicle to the inside of the scrotum so it cannot reascend.

The primary risks of orchiopexy are excessive bleeding and INFECTION, both of which are uncommon. Recovery is typically rapid, with HEALING complete within two weeks. When done early in childhood, orchiopexy preserves FERTILITY. However, an increased risk for TESTICULAR CANCER remains, making TESTICULAR SELF-EXAMINATION an important screening procedure.

See also ORCHIECTOMY; SURGERY BENEFIT AND RISK ASSESSMENT; TESTICLES.

orchitis INFLAMMATION of one testicle or both TESTICLES, often due to INFECTION. Bacterial infection may result from SEXUALLY TRANSMITTED DISEASES (STDs) such as GONORRHEA or SYPHILIS. MUMPS, a viral INFECTION that primarily affects the SALIVARY GLANDS, is a common cause of orchitis, particularly when the mumps VIRUS infects adult men.

The symptoms of orchitis are PAIN and swelling of the involved testicle. The diagnostic path includes physical examination of the SCROTUM and testicles and sometimes ULTRASOUND to rule out other causes of similar symptoms such as TESTICULAR TORSION, HYDROCELE, or VARICOCELE.

Treatment with ANTIBIOTIC MEDICATIONS is necessary when the infection is bacterial. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) relieve pain and inflammation regardless of the cause. Resting in a reclining position or wearing an athletic supporter also provides relief. A complication of orchitis may be testicular atrophy (reduced size of the affected testicle), which may affect SPERM production and FERTILITY. An atrophied testicle also presents an increased risk for TESTICULAR CANCER, making routine TESTICULAR SELF-EXAMINATION prudent.

See also BACTERIA; EPIDIDYMITIS.

orgasm Intense sensation of pleasure and excitement that occurs at the culmination of sexual stimulation. Involuntary contractions of the pelvic muscles typically accompany orgasm. In men these contractions result in EJACULATION, propelling SEMEN from the urethral opening (meatus) at the

tip of the **PENIS**. In women the contractions of orgasm occur as rhythmic waves along the walls of the **VAGINA**. Aside from being a source of intense pleasure, orgasm appears to serve as a mechanism to facilitate the movement of **SPERM** through the vagina. This is important from a reproductive perspective as the vagina presents a fairly hostile environment for sperm, which are not able to survive longer than an hour or two within it.

Though a man can have an orgasm without ejaculating, he cannot ejaculate without orgasm. After orgasm a man enters a refractory period during which his body recovers from the experience. During this time the mechanism of **ERECTION** does not respond to sexual stimulation and many men feel the overwhelming desire to fall asleep. The length of the refractory period varies with age and among men, ranging from 10 to 20 minutes for a man in his 20s to an hour or longer for a man 50 or older. A woman does not have a refractory period and may continue or revive sexual arousal indefinitely. The consistent inability to reach orgasm is a form of **SEXUAL DYSFUNCTION** that may have physiologic or emotional foundations.

See also [ERECTILE DYSFUNCTION](#); [MASTURBATION](#); [RETROGRADE EJACULATION](#); [SEXUAL INTERCOURSE](#).

ova The female cells of reproduction, also called eggs or gametes. An ovum, also called an oocyte (single egg cell), is a haploid cell; it contains one half of the genetic material necessary for human life. At birth the **OVARIES** contain about 400,000 follicles, each of which holds a single immature ovum. At **PUBERTY** the follicles begin to ripen, with usually one ovum coming to maturity with each **MENSTRUAL CYCLE**. Over the course of a woman's reproductive years her ovaries produce 400 to 600 ripened ova. About 10 to 20 times as many ova begin but do not complete the maturation process. The ovaries eventually absorb ova that fail to reach maturity.

Ovulation The sequence of hormonal and physiologic changes that bring an ovum to maturity is **OVULATION**, which takes place during the start of the menstrual cycle's luteal phase around day 14 of the menstrual cycle (day 1 being the first day of **MENSTRUATION**). The **PITUITARY GLAND** releases first a surge of **FOLLICLE-STIMULATING HORMONE (FSH)**, which activates an ovarian follicle. The

follicle secretes **ESTROGENS**, which begin the maturation process for the ovum the follicle contains. The pituitary gland then secretes **LUTEINIZING HORMONE (LH)**, which induces the ovarian follicle to produce **PROGESTERONE**. The progesterone brings the ovum to full maturity and the follicle ruptures, releasing the ovum for capture into the fallopian tube.

Fertilization, implantation, and conception

The smooth **MUSCLE** walls of the fallopian tube contract in a gentle, wavelike pattern that draws the ovum through the tube toward the **UTERUS**. When **SPERM** are also present in the fallopian tube, fertilization takes place. Typically, though many sperm attempt to penetrate the outer membrane of the ovum only one succeeds. The chemical composition of the ovum's membrane alters once the sperm is within the ovum, preventing other sperm from following. The nuclei of the gametes (ovum and sperm) fuse to form a single diploid cell, called a **ZYGOTE**. As the zygote moves along the fallopian tube toward the uterus it continues to grow and divide. By the time the zygote reaches the uterus it has become a two-layered mass of cells called a blastocyst. The outer layer of the blastocyst attaches to the endometrium; as pregnancy continues this layer becomes the **PLACENTA** and the inner layer develops into the **EMBRYO**. The completion of fertilization and implantation is **CONCEPTION**.

For further discussion of the ova within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also [ASSISTED REPRODUCTIVE TECHNOLOGY \(ART\)](#); [CELL STRUCTURE AND FUNCTION](#); [FALLOPIAN TUBES](#); [FERTILITY](#); [GAMETE](#); [INFERTILITY](#); [PREGNANCY](#); [SECONDARY SEXUAL CHARACTERISTICS](#); [SEXUAL HEALTH](#).

ovarian cancer A malignant (cancerous) tumor that develops in the tissues of the ovary. Ovarian cancer may arise from any of the ovary's three types of cells—germ, stromal, and epithelial—though about 90 percent of ovarian cancers arise from the ovarian epithelium (the membranous covering of the ovary). Ovarian epithelial cancer occurs most commonly in women over age 60 (after **MENOPAUSE**). Though tumors are typically noncancerous or cancerous, ovarian epithelial

tumors may straddle the border. Doctors classify such tumors as low malignant potential (LMP); though cancerous these tumors grow slowly, have little propensity to metastasize (spread) and usually respond very well to treatment. Ovarian epithelial cancer that develops in women under age 60 is often LMP. Ovarian germ cell cancer and ovarian stromal cell cancer are rare; they are more likely to occur in women under age 50 (before menopause).

Doctors in the United States diagnose ovarian cancer in about 22,000 women each year. Because ovarian cancer typically causes few symptoms until it has metastasized (spread), the prognosis (outlook) for ovarian cancer overall is rather bleak. However, early diagnosis allows successful treatment and a promising outlook. Any woman who has her OVARIES is vulnerable to ovarian cancer, even if she has had a HYSTERECTOMY (OPERATION to remove the UTERUS). Bilateral OOPHORECTOMY (operation to remove both ovaries) ends the risk for ovarian cancer, though it remains possible for epithelial cancer very much like ovarian cancer to develop in the peritoneum, the membranous lining of the abdominal cavity.

Symptoms and Diagnostic Path

Early symptoms of ovarian cancer are often generalized and vague. Both the woman and her doctor commonly mistake them for symptoms of gastrointestinal disorders. These early symptoms may include

- sensation of abdominal bloating
- abdominal swelling
- unexplained weight gain
- changes in bowel habits (CONSTIPATION OR DIARRHEA)
- urinary urgency

As ovarian cancer progresses, symptoms become more specific and include

- pelvic, abdominal, or low BACK PAIN
- unexplained weight loss
- unusual vaginal bleeding
- fatigue and general sense of not feeling well (malaise)

- persistent gastrointestinal symptoms (NAUSEA, VOMITING, diarrhea, or constipation) that do not vary with eating patterns

The diagnostic path includes comprehensive medical examination including PELVIC EXAMINATION, BLOOD tests (cell count and differentiation as well as CA-125), abdominal ULTRASOUND or COMPUTED TOMOGRAPHY (CT) SCAN, and often COLONOSCOPY.

Blood levels of the protein CA-125 are often elevated in moderate to advanced ovarian cancer though not in early ovarian cancer. As well, numerous noncancerous conditions can elevate CA-125 blood levels. Though the doctor may consider the CA-125 level among the diagnostic indicators, it does not alone confirm or rule out diagnosis of ovarian cancer. Other tumor markers include ALPHA-FETOPROTEIN (AFP), HUMAN CHORIONIC GONADOTROPIN (hCG), and CARCINOEMBRYONIC ANTIGEN (CEA).

Because benign tumors and cysts of the ovaries are common, noninvasive diagnostic procedures often cannot determine whether an ovarian growth is cancerous or noncancerous. The only certain diagnostic procedure is laparoscopy or laparotomy, both of which are surgical operations to enter the abdominal cavity, to view the ovary and remove samples of tissue (biopsy). Laparoscopy is a MINIMALLY INVASIVE SURGERY in which the surgeon uses several small incisions through which he or she inserts an endoscope (flexible, lighted viewing instrument) and specialized instruments to visualize the ovary via display on a monitor. Laparotomy is an OPEN SURGERY in which the surgeon makes a substantial incision through the SKIN in the abdomen and examines the ovary directly.

The pathologist who examines the tissue samples determines the type of cancer cells that are present and assesses the extent to which they are likely to have spread to locations outside the ovary. The results of this assessment, called STAGING AND GRADING OF CANCER, help guide treatment decisions. The pathologist also may revise the stage or grade may change after surgery to remove the cancer, depending on the surgeon's findings and the character of the cancer cells within the tumor.

BASIC STAGING OF OVARIAN CANCER

Stage	Meaning	Treatment Options
low malignant potential (LMP)	tumor is borderline cancerous and slow growing	surgery to remove the involved ovary (unilateral OOPHORECTOMY)
stage 1	cancer remains confined to a local tumor in one ovary	surgery (bilateral salpingo-oophorectomy, total HYSTERECTOMY, omentectomy, and lymphadenectomy) intraperitoneal CHEMOTHERAPY, RADIATION THERAPY with follow-up single DRUG chemotherapy, or combination (multiple drug) chemotherapy
stage 2	cancer involves both OVARIES or has spread to the FALLOPIAN TUBES, UTERUS, or tissue within the pelvis	surgery (bilateral salpingo-oophorectomy, total hysterectomy, omentectomy, and LYMPH NODE dissection) combination chemotherapy, four to six cycles
stage 3	cancer has spread to other organs in the abdomen, the peritoneum, and abdominal LYMPH nodes	surgery (bilateral salpingo-oophorectomy, total hysterectomy, omentectomy, and lymph node dissection) and debulking surgery combination chemotherapy, four to six cycles
stage 4	cancer has spread to distant organs	debulking surgery combination chemotherapy, multiple cycles “second look” surgery to remove remaining cancerous tissue
stage 4/recurrent	cancer has returned after treatment	combination chemotherapy IMMUNOTHERAPY clinical trial of appropriate investigational new treatments high-DOSE chemotherapy with autologous bone marrow therapy (STEM CELL support) palliative surgery for symptom relief

Treatment Options and Outlook

The treatment of first choice for nearly all ovarian cancers is surgery to remove the ovary that contains the tumor. In all ovarian cancers except LMP, surgery also includes removal of the rest of the pelvic reproductive organs—both ovaries, both FALLOPIAN TUBES, uterus, and CERVIX—as well as the omentum (a layer of fatty tissue that covers the interior of the peritoneum) and nearby LYMPH nodes (lymphadenectomy). Because ovarian cancer tends to spread in layers of cells that cover the pelvic or abdominal structures, the surgeon removes as much of it as possible through a proce-

dure called debulking. Debulking may also involve removing segments of the SMALL INTESTINE. Most women also receive adjuvant therapy (follow-up treatment) with CHEMOTHERAPY, RADIATION THERAPY, or both. Treatment with a single chemotherapy agent is often sufficient to treat early stage 1 ovarian cancer, though many oncologists prefer combination chemotherapy or radiation therapy with single-agent chemotherapy after. Multiple cycles of combination chemotherapy are the current standard of treatment for stage 2 through stage 4/recurrent ovarian cancer. Some chemotherapy agents are available in oral forms

(pills), which a woman can take at home, and others are available only in intravenous injectable forms, which require administration at a chemotherapy center.

CHEMOTHERAPY AGENTS TO TREAT OVARIAN CANCER

cisplatin	doxorubicin
etoposide	ifosfamide
melphalan	paclitaxel
topotecan	

High-dose chemotherapy with autologous BONE MARROW therapy, also called STEM CELL support, is often effective in providing short-term REMISSION in stage 4 ovarian cancer. However, many cancer experts question whether the high risk and cost of this treatment ultimately improves a woman's QUALITY OF LIFE and LIFE EXPECTANCY. For many women, investigational treatments provide equal or better results with significantly less severe side effects and complications.

Because the spread of ovarian cancer within the abdominal cavity is so diffuse, early detection and treatment are particularly essential. Surgery is most effective when the tumor remains confined to the ovary; treatment is most effective when the surgeon is able to remove all of the cancer. The outlook for remission with early treatment is very good. Later stage ovarian cancer is difficult to control because the surgeon cannot remove all of the cancer. Chemotherapy provides highly effective treatment though side effects can be significant. Later stage ovarian cancer has a tendency to recur after remission, though each period of remission may last three to five years.

Risk Factors and Preventive Measures

The primary risk factors for ovarian cancer are age greater than 60 years and family history of ovarian cancer, especially among first-degree relatives (mother, daughter, sister). Women who carry the BRCA-1/BRCA-2 GENE mutations have especially high risk, though not the certainty, to develop ovarian cancer. Some women who have such high risk choose prophylactic oophorectomy (surgery to remove the ovaries) when they reach the end of their childbearing years or menopause as a means for reducing their risk.

The causes of ovarian cancer are unclear, though there appear to be hormonal correlations. Women who carry at least one pregnancy to delivery, breastfeed, or take oral contraceptives (birth control pills) for longer than three years, or have a TUBAL LIGATION or a total hysterectomy (surgery to remove the uterus and cervix) for reasons other than cancer appear significantly less likely to develop ovarian cancer. Lifestyle factors such as the fat content of the diet and the frequency of physical exercise also correlate to the risk for ovarian cancer, with the risk much lower in women who eat a low-fat diet and get daily physical exercise (minimum 30 to 60 minutes). Cigarette smoking raises the risk for ovarian cancer, as it does for many cancers.

Though many ovarian tumors are difficult to palpate (feel), health experts recommend routine pelvic examination as a means of possible early detection of ovarian cancer. However, the PAP TEST that often accompanies a pelvic examination, while very effective for detecting early CERVICAL CANCER, does not detect ovarian cancer. The schedule of examination varies with age and health status, though women at high risk for ovarian cancer should have annual pelvic examinations.

See also BREAST CANCER; CANCER TREATMENT OPTIONS AND DECISIONS; COLORECTAL CANCER; ENDOMETRIAL CANCER; ENDOSCOPY; SURGERY BENEFIT AND RISK ASSESSMENT.

ovarian cyst A noncancerous, fluid-filled growth that forms within an ovary. Ovarian cysts are common and many are transient (come and go). The most common type of ovarian cyst is a follicular cyst, which develops in an ovarian follicle. Typically the follicle fills with fluid. Over time the fluid reabsorbs into the follicle and the cyst goes away. Sometimes a follicular cyst ruptures, causing sudden PAIN. Cysts may also form in the corpus luteum, the structure of endocrine tissue that supports a ripened ovum. Such a cyst, called a luteal cyst, typically goes away when the corpus luteum involutes (turns in on itself) and becomes absorbed into the ovarian follicle immediately preceding MENSTRUATION. Follicular cysts and luteal cysts are usually functional—that is, they come and go with the hormonal shifts of the MENSTRUAL

CYCLE. Ovarian cysts are occasionally pedunculated (growing on the end of stalks). Such cysts may twist on their peduncles and become gangrenous, which is an emergency situation requiring surgery.

Dermoid cysts, also called teratomas or germ cell cysts, are much less common though more troublesome because they can grow quite large. The key characteristic of a dermoid cyst is that it consists primarily of epithelial tissue though may also contain fatty tissue and fragments of HAIR, CARTILAGE, BONE, and sometimes TEETH. Dermoid cysts are congenital (present from birth). Doctors do not know how they occur though believe they arise from cells that escape migration when the three layers of the early EMBRYO (mesoderm, ectoderm, and endoderm) develop.

The doctor detects most ovarian cysts incidentally during routine PELVIC EXAMINATION or ULTRASOUND of the lower abdomen done for other reasons. When a woman does have symptoms they are often nonspecific in nature, such as abdominal bloating or pressure, CONSTIPATION, URINARY INCONTINENCE or URINARY FREQUENCY, or pain during SEXUAL INTERCOURSE (dyspareunia). Abdominal or transvaginal ultrasound or abdominal COMPUTED TOMOGRAPHY (CT) SCAN help the doctor confirm the diagnosis. When these diagnostic imaging procedures are not conclusive, the doctor may perform diagnostic laparoscopy to look at the cyst and take a tissue sample for biopsy.

Most ovarian cysts go away without treatment or intervention. The gynecologist may recommend surgical removal of an ovarian cyst that is large, persistent, or symptomatic (causes discomfort, irregular menstrual periods, or bleeding) or when the cyst has suspicious features that cause the gynecologist to want to rule out OVARIAN CANCER. Though ovarian cysts are not cancerous and very seldom become cancerous, they can co-exist with cancerous tumors. As well, ovarian cancer tumors commonly have cystic characteristics. Often it is possible to remove the cyst without damaging the ovary. When the cyst is large or questionable the surgeon may need to remove the entire ovary (OOPHORECTOMY). As long as the remaining ovary is healthy and functional, removing a single ovary does not affect the menstrual cycle or FERTILITY.

See also OVARIES; SURGERY BENEFIT AND RISK ASSESSMENT.

ovaries The female organs of reproduction, also called the female gonads. The ovaries produce OVA (eggs) and sex hormones, predominantly ESTROGENS and PROGESTERONE as well as small amounts of ANDROGENS. A woman has two ovaries, one ovary on each side of the UTERUS in the lower abdomen. Ligaments suspend the ovaries in place within the abdominal cavity. Each ovary is about the size, shape, and consistency of a large olive. At birth it contains the full complement of ova that will supply a woman for all her years of FERTILITY.

The ovary has two distinct layers of structure, an outer cortex and an inner medulla. The ovarian cortex contains the ovarian follicles, each of which holds an immature ovum (egg), also called a GAMETE or germ cell. The fibrous tissue of the ovarian medulla, made up of stroma cells, contains the ovary's BLOOD vessels, LYMPH vessels, and nerves. The layer of cells covering the ovary is the epithelium; it is made up of epithelial cells (the same type of cell that makes up the SKIN and mucous membranes throughout the body).

Beginning during PUBERTY with the onset of MENSTRUATION, hormonal influences ripen one ovum (sometimes called an oocyte) each MENSTRUAL CYCLE. The ovary releases the ovum into a pocket of fluid that surrounds it. The fimbriae of the fallopian tube (fluted edges of the tube's open end) float in this fluid, extending toward but not touching the ovary. The undulating movements of the fimbriae pull the released ovum into the fallopian tube where, if SPERM are also present, fertilization may occur.

The PITUITARY GLAND releases FOLLICLE-STIMULATING HORMONE (FSH) and LUTEINIZING HORMONE (LH) at different phases of the menstrual cycle to stimulate the sequence of events that will cause the maturation of an ovum. Several ova typically begin the maturation process during each menstrual cycle though usually only one will complete it. The follicle expels the mature, or ripe, ovum. The cells of the follicle produce estrogens and proteins. The developing ovum is a haploid cell—that is, it contains precisely one half the complement of chromosomes (23) necessary to support human

life. When the ovum merges with the sperm, the resulting ZYGOTE contains the full complement of chromosomes (46).

HEALTH CONDITIONS THAT AFFECT THE OVARIES

ENDOMETRIOSIS	OVARIAN CANCER
OVARIAN CYST	POLYCYSTIC OVARY SYNDROME
PREMATURE OVARIAN FAILURE	(PCOS)
(POF)	TURNER'S SYNDROME

For further discussion of the ovaries within the context of the structures and functions of reproduction and sexuality, please see the overview section “The Reproductive System.” For further discussion of the ovaries within the context of the structures and functions of the endocrine system, please see the overview section “The Endocrine System.”

See also CELL STRUCTURE AND FUNCTION; [CONCEPTION](#); [CONTRACEPTION](#); [PREGNANCY](#); [TESTICLES](#).

ovulation The maturation and release of an ovum (egg) during a woman’s monthly MENSTRUAL CYCLE. Ovulation establishes FERTILITY (the physiologic ability to conceive a PREGNANCY); only during ovulation may pregnancy occur. Ovulation marks the transition from the proliferative phase to the luteal phase of the menstrual cycle, during which the PITUITARY GLAND’s release of LUTEINIZING HORMONE (LH) stimulates the ovarian follicle (sometimes called the graafian follicle) to rupture. The follicle

expels the ripened ovum into a small pool of fluid that surrounds the ovary. The fimbriae (fluted edges of the fallopian tube) float in this fluid. As the fimbriae undulate they draw the ovum toward them and into the fallopian tube, where contractions of the tube’s wall propel the ovum along the fallopian tube toward the UTERUS. FERTILIZATION, if it is to occur, takes place in the fallopian tube.

It is very difficult to calculate or determine the timing of ovulation. Though ovulation generally occurs within 10 to 15 days after the start of the previous menstrual period, its timing depends on numerous factors, most of which are hormonal. Body temperature rises slightly and the quality of cervical mucous changes during ovulation. Home ovulation testing kits can determine ovulation with fair accuracy; laboratory tests done through the doctor’s office are more precise. Ovulation timing is important for women who are trying to conceive, and also for women who are trying to avoid conception. The rhythm method, also called periodic abstinence, relies on avoiding SEXUAL INTERCOURSE during ovulation as a means of CONTRACEPTION.

For further discussion of ovulation within the context of the structures and functions of reproduction and sexuality, please see the overview section “The Reproductive System.”

See also [ASSISTED REPRODUCTIVE TECHNOLOGY \(ART\)](#); [CERVIX](#); [FALLOPIAN TUBES](#); [MENSTRUATION](#); [MITTELSCHMERZ](#); [OVARIES](#).

Paget's disease of the breast A rare presentation of BREAST CANCER, also called Paget's disease of the nipple. Researchers believe Paget's disease of the BREAST occurs when disordered cells from a cancer within the breast migrate to the SKIN surface, most likely through the milk ducts, to infiltrate the tissues of the outer breast and the nipple. Paget's disease of the breast is most commonly associated with an underlying invasive breast cancer or ductal cancer in situ (DCIS).

The symptoms of Paget's disease of the breast may develop over months to years, and typically begin with a scaly RASH that may itch or burn. The skin of the nipple and the areola (the area around the nipple) may crack and bleed. Because skin conditions such as atopic DERMATITIS (also called eczema) and PSORIASIS commonly affect the breasts, early symptoms are often misdiagnosed as dermatologic. One subtle difference is that Paget's disease of the breast begins in the nipple and spreads to the areola, whereas dermatologic conditions begin in the areola and extend to the nipple. As Paget's disease of the breast advances, the nipple may invert or there may be bloody discharge from the nipple.

The diagnostic path typically includes MAMMOGRAM (X-RAY of the breast) and biopsy of the cells of the nipple and underlying breast tissue. ULTRASOUND of the breast may reveal tumors within the breast. Treatment begins with surgery to remove the cancer, which may be breast-conserving surgery when the cancer remains fairly localized and simple or radical MASTECTOMY when the cancer is widespread within the breast. RADIATION THERAPY, HORMONE THERAPY (such as with tamoxifen) when the underlying cancer is hormone sensitive, and CHEMOTHERAPY are common adjuvant (follow-up) treatments.

See also CANCER TREATMENT OPTIONS AND DECISIONS; PAGET'S DISEASE OF THE BONE.

Pap test A screening test for disorders of the CERVIX, notably CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN) and CERVICAL CANCER. A Pap test, also called a Papanicolaou test, is the laboratory examination of cells swabbed from the cervix during a PELVIC EXAMINATION. The test derives its name from the doctor who developed it. Women over age 18 should have Pap tests every one to three years, depending on their health status. A woman who has had a total HYSTERECTOMY (surgical removal of the UTERUS including the cervix) for reasons other than cancer does not need Pap tests unless she has a history of HUMAN PAPILLOMAVIRUS (HPV). When the hysterectomy was for cancer or was a simple hysterectomy (removal only of the uterus), the woman needs Pap tests according to routine recommendations.

See also COLPOSCOPY.

paraphimosis A condition in which the foreskin retracts onto the shaft of the PENIS and will not return to its normal position to cover the glans (tip of the penis). Paraphimosis can only occur in an uncircumcised man. The foreskin swells and acts as a tourniquet, constricting the flow of BLOOD and causing the shaft of the penis to engorge while cutting off the blood supply to the glans. Paraphimosis requires immediate medical attention to prevent permanent damage, including GANGRENE that necessitates AMPUTATION, to the penis.

Treatment for paraphimosis includes measures to reduce swelling such as ice and compression dressings to the penis. Injection of hyaluronidase, an enzyme, often rapidly reduces the swelling (edema). Once the swelling goes down the doctor may then gently manipulate the foreskin back

PAP TEST RECOMMENDATIONS		
Woman's Age	Health Status	Pap Test Interval
under 21	sexually active	every year
21 to 30	all women regardless of health status	every year
31 to 64	three consecutive normal Pap tests no SEXUALLY TRANSMITTED DISEASES (STDs)	every two to three years
31 to 64	multiple sex partners HUMAN PAPILLOMAVIRUS (HPV) INFECTION abnormal Pap test within three years has had treatment for cancer of the CERVIX or endometrium (UTERUS)	every year
65 to 70	normal Pap tests for the previous 10 consecutive years total HYSTERECTOMY	no longer necessary
any age	mother took diethylstilbestrol (DES) when she was pregnant HIV positive organ transplant recipient long-term corticosteroid therapy impaired immune function	every year

over the glans. When these measures are inadequate, the doctor may make an incision through the foreskin to release it. The definitive treatment for paraphimosis is CIRCUMCISION (surgical removal of the foreskin).

See also PHIMOSIS.

pelvic examination A manual and visual examination of a woman's VULVA, VAGINA, and CERVIX. A routine pelvic examination has three parts: visual examination of the external GENITALIA, bimanual palpation, and speculum examination of the inner vagina and the cervix. A pelvic examination is painless and is part of a ROUTINE MEDICAL EXAMINATION for women beginning around age 18 and continuing throughout life. For a routine pelvic examination a woman lies on her back on the examination table with her feet in stirrups and her knees spread apart. The doctor also performs pelvic examination during labor to assess the status of the cervix and progression of labor.

Visual examination The doctor visually examines the external genitalia to detect abnormalities

such as growths, sores, discoloration, and other indications of INFECTION or disease.

Bimanual examination For the bimanual portion of the pelvic exam the doctor inserts two gloved and lubricated fingers into the vagina and with the other hand palpates the outside of the abdomen. This procedure allows the doctor to feel the size and placement of the UTERUS and the OVARIES, which may detect abnormalities such as swelling, hypersensitivity or PAIN, displacement (such as tipped uterus), and other indications of health concerns.

Speculum examination The doctor then inserts a lubricated speculum into the vagina. The speculum has two opposing blades that fit together to form a smooth, thin blade that easily enters the vagina. Once the speculum is in position the doctor gently opens the blades to spread apart the walls of the vagina, providing access to the cervix. The doctor visually examines the cervix and inner vagina with the aid of a bright light, and may take a cervical smear (sampling of cells and mucous from the cervix) for a PAP TEST or other laboratory

procedures. The doctor closes the speculum’s blade to withdraw the speculum.

See also [KEGEL EXERCISES](#); PREVENTIVE HEALTH CARE AND IMMUNIZATIONS.

pelvic inflammatory disease (PID) A bacterial INFECTION involving the UTERUS, FALLOPIAN TUBES, CERVIX, and VAGINA. Untreated PID has the potential to become life threatening if it spreads to involve the peritoneal membrane (PERITONITIS), the tissue that encloses the abdominal cavity. Because PID can cause scarring within the fallopian tubes that occludes them (blocks the tubes’ openings), chronic or recurrent PID is a leading cause of INFERTILITY in women. PID is a significant health concern in the United States with doctors diagnosing more than one million women with it each year, about half of whom have permanently impaired FERTILITY as a consequence.

The most common cause of PID is recurrent or untreated infection with SEXUALLY TRANSMITTED DISEASES (STDs) such as CHLAMYDIA and GONORRHEA. Other causes include infection that occurs as a postoperative complication after a surgical procedure such as DILATION AND CURETTAGE (D&C) or elective ABORTION. A less common cause of PID is infection resulting from an intrauterine device (IUD), a form of long-term birth control.

Symptoms and Diagnostic Path

It is possible to have PID, especially chronic PID, with few or no symptoms. Many women who have PID typically appear quite ill, however, and may have FEVER and chills in addition to other symptoms. Such symptoms may include

- yellowish or greenish malodorous (foul-smelling) vaginal discharge
- lower abdominal tenderness, cramping, or PAIN
- NAUSEA, VOMITING, and DIARRHEA
- vaginal bleeding between menstrual periods
- irregular or unusually heavy menstrual periods

The diagnostic path includes PELVIC EXAMINATION with vaginal discharge and tissue samples for laboratory analysis and BLOOD tests to evaluate the presence of infection or INFLAMMATION within the body (such as elevated sedimentation rate, white

blood cell count, and C-REACTIVE PROTEIN). The cervix and uterus are generally very tender to palpation during the pelvic exam, which is a key diagnostic criterion.

Treatment Options and Outlook

Treatment is prompt administration of ANTIBIOTIC MEDICATIONS, by intravenous (IV) or intramuscular injection for severe symptoms and orally otherwise. Antibiotic therapy may include two or more antibiotic medications, depending on the identified BACTERIA present in the vaginal and cervical cultures. It is essential to take the full course of all antibiotics as prescribed to completely eradicate the infection, which cures the PID. ANALGESIC MEDICATIONS relieve pain and reduce fever to improve comfort. Possible complications of PID include infertility, increased risk for ECTOPIC PREGNANCY, and chronic pelvic pain. The likelihood of these complications increases with each episode of PID, though prompt diagnosis and treatment helps mitigate their risk.

ANTIBIOTICS TO TREAT PELVIC INFLAMMATORY DISEASE (PID)	
ampicillin/sulbactam	cefotetan
cefoxitin	ceftriaxone
ciprofloxacin	clindamycin
doxycycline	gentamicin
metronidazole	ofloxacin

Risk Factors and Preventive Measures

The primary risk factor for PID is untreated STD infection. Many people do not have symptoms of STDs yet are infected and pass the infections to their sex partners. Multiple sex partners and unprotected sex are high-risk behaviors for STDs and PID. Measures to prevent infection among sexually active adults include mutual monogamy and latex condom use with every sexual act.

See also HIV/AIDS; [MENSTRUATION](#); SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION.

penis The male organ for URINATION and SEXUAL INTERCOURSE. The penis is an elongated, cylindrical structure made of connective and erectile tissue that extends outside the body from the base of the pelvis. Ligaments attach the root of the penis (segment within the body) to the pubic bone at the

front of the pelvis and the ischial bones at the back of the pelvis. The shaft is the length of the penis that extends outward from the body, and the glans is the end or head of the penis. The URETHRA exits the glans through an opening called the urethral meatus. A loose fold of SKIN, the foreskin (also called the prepuce), covers the glans at birth; beginning around 8 years of age the foreskin retracts from the glans when the penis is erect and returns to drape the glans when the penis is flaccid. CIRCUMCISION is a surgical OPERATION to remove the foreskin.

The interior penis contains three channels: the corpus spongiosum runs along the underside of the penis and houses the urethra; the two corpora cavernosa run side-by-side along the top of the penis and engorge with BLOOD to stiffen and enlarge the penis during ERECTION. A wall of fibrous tissue, the septum, separates and supports the corpora cavernosa. The inside of each corpus cavernosum is a honeycombed network of spaces (called trabeculae) that fill with blood when the penis is erect. The erect penis is capable of penetrating the woman's VAGINA during SEXUAL INTERCOURSE, with sexual stimulation culminating in ORGASM and EJACULATION.

HEALTH CONDITIONS THAT CAN AFFECT THE PENIS

BALANITIS	CANCER OF THE PENIS
CHORDEE	EPISPADIAS
ERECTILE DYSFUNCTION	GENITAL HERPES
HUMAN PAPILLOMAVIRUS (HPV)	HYPOSPADIAS
HYPOGONADISM	KLINEFELTER'S SYNDROME
PARAPHIMOSIS	PEYRONIE'S DISEASE
PHIMOSIS	PRIAPISM

For further discussion of the penis within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also OVARIES; SEXUAL DYSFUNCTION; SEXUAL HEALTH.

perimenopause The period of time during which a woman's body transitions from FERTILITY to MENOPAUSE. The length of perimenopause varies widely though tends to be five to seven years. Perimenopause begins with the changes in the MENSTRUAL CYCLE that herald the approach of

menopause. These changes include irregular spacing of menstrual periods (including skipped periods), unusually heavy or light menstrual flow, light breakthrough bleeding (bleeding between periods), and HOT FLASHES.

Bleeding between periods may indicate a health condition that requires treatment. A doctor should evaluate breakthrough bleeding to determine whether it is normal.

Because PREGNANCY is possible during perimenopause, as OVULATION may occur intermittently, a woman who has two consecutive skipped menstrual periods should have a pregnancy test. Women typically experience a range of fluctuating discomforts, notably hot flashes and sleep disturbances, during the menopausal transition. Menopause is a point in time identified in retrospect as the complete absence of menstrual periods for 12 consecutive months.

See also DYSFUNCTIONAL UTERINE BLEEDING (DUB); ENDOMETRIOSIS; MENSTRUATION; UTERINE FIBROIDS.

Peyronie's disease A condition in which a hardened, fibrous plaque forms within the connective tissue of the PENIS, causing a contracture that pulls the penis into a curved position. Researchers do not know what causes the plaque to form. Some believe it represents an autoimmune response (overreaction of the IMMUNE SYSTEM) and others that it occurs as a reaction to traumatic injury. Peyronie's disease generally affects men age 50 and older. The contracture often causes PAIN, particularly when the penis is erect, and interferes with or prevents SEXUAL INTERCOURSE.

The doctor can usually diagnose Peyronie's disease on physical examination of the penis. The plaque is both visible and palpable. The doctor may request an ULTRASOUND of the penis, which shows the extensiveness of the plaque. In about a third of men who have Peyronie's disease the plaque softens and goes away on its own. In other men the curvature progresses to a certain point and then remains stable. It is important to evaluate the potential risks compared to benefits for proposed treatments, which include injecting the plaque with a medication to dissolve the fibrous

tissue and surgery to remove the plaque. A key risk of either procedure is ERECTILE DYSFUNCTION (inability to obtain erections). Generally these treatments are most appropriate when the con-
tracture completely prevents sexual intercourse.

See also CHORDEE; PARAPHIMOSIS; PHIMOSIS; PRI-
APISM.

phimosis A condition in which the foreskin becomes fused to the glans of an uncircumcised PENIS and will not retract. Phimosis occasionally occurs as a congenital condition (present at birth) though more often develops later in life, typically as a consequence of poor PERSONAL HYGIENE. Phi-
mosis is the leading cause of BALANITIS, a fungal INFECTION of the inner surface of the foreskin, and can interfere with URINATION and cause PAIN with ERECTION. Recurrent phimosis increases a man's risk for CANCER OF THE PENIS.

The doctor is sometimes able to gently free the adhered foreskin after anesthetizing the penis. Frequent retraction of the foreskin and diligent cleansing are necessary to prevent phimosis from recurring. When this is not effective or phimosis becomes chronic, the recommended treatment is CIRCUMCISION, an OPERATION to surgically remove the foreskin. Though in some men an unusually tight foreskin (congenital phimosis) is the primary cause of phimosis, diligent personal hygiene can prevent most phimosis. It is important for uncir-
cumcised boys and men to clean beneath the fore-
skin every day by retracting the foreskin, washing the glans gently but thoroughly to remove any accumulated secretions, and allowing the foreskin to return to its natural position.

See also CHORDEE; CONGENITAL DISORDERS; PARAPHI-
MOSIS; PEYRONIE'S DISEASE.

placenta An organ of PREGNANCY that nourishes and sustains the FETUS. The placenta also secretes a number of hormones that maintain the biochemi-
cal environment within the woman's body to sup-
port the pregnancy. The placenta develops within the first two weeks after the blastocyst implants into the endometrium of the UTERUS, arising from the outer layer of the blastocyst's cells, the tro-
phoblast. The amniotic sac, which encloses the developing fetus, and the UMBILICAL CORD also arise from the trophoblast.

PLACENTAL HORMONES

activin	chorionic adrenocorticotropin
CHORIONIC GONADOTROPIN	chorionic somatomammotropin
CORTICOTROPIN-RELEASING	CORTISOL
HORMONE (CRH)	ESTROGENS
GONADOTROPIN-RELEASING	GROWTH HORMONE-RELEASING
HORMONE (GNRH)	HORMONE (GHRH)
INHIBIN	placental actinogen
PROGESTERONE	PROLACTIN
RELAXIN	THYROTROPIN-RELEASING HORMONE
	(TRH)

The placenta uniquely belongs to both the mother and the fetus. Though the maternal BLOOD circulation delivers NUTRIENTS and oxygen to the fetal blood circulation and carries away fetal wastes, the two circulations do not normally mix with each other. The side of the placenta that faces the fetus is the chorion. Fringelike extensions called the chorionic villi permeate the tissue of the maternal portion of the placenta. Fetal blood circulates through the chorionic villi. Arterioles (tiny arteries) and venules (tiny veins) extend from the myometrium (muscular wall of the uterus) into the spaces between the chorionic villi. The arteri-
oles carry maternal blood into the spaces where it circulates around the chorionic villi. Nutrients, oxygen, and wastes pass across the thin mem-
branes that enclose the chorionic villi.

Problems that can arise with the placenta dur-
ing pregnancy include

- placenta abruptio (also called placental abrup-
tion), in which the placenta partially or com-
pletely separates from the uterus; partial
separation reduces nutrition to the fetus and
complete separation is fatal to the fetus
- placenta accreta, in which the tissues that
anchor the placenta to the wall of the uterus
penetrate the myometrium too deeply, making
it difficult for the placenta to separate after
birth
- placenta previa, in which the placenta grows
partially or completely across the CERVIX, nec-
essitating CESAREAN SECTION to prevent hemor-
rhage during labor

After the fetus is born a second round of con-
tractions separate the placenta from the uterine

wall and expel it through the VAGINA. The expelled placenta is the afterbirth.

For further discussion of the placenta within the context of the structures and functions of reproduction and sexuality, please see the overview section “The Reproductive System.”

See also AMNIOCENTESIS; AMNIOTIC FLUID; CHILD-BIRTH; CHORIONIC VILLI SAMPLING (CVS); CONCEPTION; HORMONE.

polycystic ovary syndrome (PCOS) A condition in which the OVARIES produce excessive ANDROGENS, the male sex hormones, resulting in irregular menstrual cycles and often anovulation (absence of egg maturation and release). A common characteristic of PCOS is the formation of multiple and often numerous cysts within the follicles of the ovaries. PCOS, sometimes called Stein-Leventhal syndrome or hyperandrogenic anovulation, is a common cause of INFERTILITY in women.

Researchers believe INSULIN RESISTANCE, an endocrine disorder in which the cells in the body do not appropriately respond to INSULIN, is a key factor in the development of PCOS though do not know the mechanisms of the relationship between the two conditions. PCOS commonly appears among a constellation of symptoms associated with insulin resistance including OBESITY, HYPERLIPIDEMIA (elevated levels of fatty acids in the BLOOD circulation), ATHEROSCLEROSIS (accumulations of fatty plaques within the walls of the arteries), CORONARY ARTERY DISEASE (CAD), and type 2 DIABETES.

Symptoms and Diagnostic Path

The symptoms of PCOS include

- irregular menstrual cycles
- AMENORRHEA (absence of MENSTRUATION) or frequent skipped menstrual periods
- excessive or male pattern body HAIR (HIRSUTISM)
- male pattern thinning of the hair on the head (ALOPECIA)
- pelvic discomfort or PAIN
- inability to conceive (infertility)
- excessive or persistent ACNE

In addition, many women who have PCOS also have HYPERTENSION (high BLOOD PRESSURE) along

with other health conditions in the insulin resistance constellation (notably diabetes, hyperlipidemia, and obesity). Though some women who have PCOS have irregular menstrual cycles from MENARCHE (the onset of menstruation) or fail to start menstruating (primary amenorrhea), many women do not suspect they have PCOS until they are unsuccessful in their attempts to become pregnant.

The diagnostic path begins with a comprehensive medical examination including blood tests to measure HORMONE levels, GLUCOSE tolerance test, and PELVIC EXAMINATION, during which the doctor often can palpate (feel) the enlargement and irregular shape of the ovaries that is typical with multiple cysts. Transvaginal or pelvic ULTRASOUND provides visual representation of the ovaries that can confirm the diagnosis.

Treatment Options and Outlook

Though there is no cure for PCOS, medical treatments to regulate the balance of hormones in the body often can restore normal OVULATION and menstruation. For women who are not trying to become pregnant, the medication of choice is an oral contraceptive (birth control pills). Some oral ANTIDIABETES MEDICATIONS that affect how cells respond to insulin are also effective at improving symptoms.

For women who are trying to become pregnant, FERTILITY medications may stimulate ovulation though the risk for multiple pregnancy becomes significant. Some doctors recommend in vitro fertilization (IVF), a method of ASSISTED REPRODUCTIVE TECHNOLOGY (ART), rather than fertility medications for women who have PCOS and wish to become pregnant because IVF allows control over the number of potential fetuses. During pregnancy women who have PCOS have increased risk for spontaneous ABORTION, GESTATIONAL DIABETES, PREECLAMPSIA, and PREMATURE BIRTH, though diligent PRENATAL CARE keeps these risks to a minimum.

A surgical treatment option is ovarian drilling, a laparoscopic OPERATION in which the surgeon uses electrocautery to burn selected ovarian follicles to destroy the cysts they contain. Ovarian drilling typically restores normal ovulation for a limited time, which reduces symptoms overall. However,

the effectiveness of ovarian drilling eventually diminishes as cysts continue to grow in the remaining ovarian follicles.

Nonmedical approaches such as electrolysis or laser hair removal can improve excessive hair growth. Daily physical exercise improves cell sensitivity to insulin, as does maintaining appropriate body weight. Weight loss of 10 to 15 percent often is enough to restore normal menstrual cycles. Weight management also improves conditions that may co-exist with PCOS such as hypertension and diabetes. Women in whom hormonal balance continues such that amenorrhea persists long term (as may occur in untreated PCOS) have increased risk for ENDOMETRIAL HYPERPLASIA and ENDOMETRIAL CANCER (overgrowth and cancer of the endometrium, the lining of the UTERUS).

Risk Factors and Preventive Measures

The primary risk factor for PCOS appears to be insulin resistance. Lifestyle measures to maintain healthy body weight and regulate the insulin–glucose balance often reduce symptoms of PCOS, though there are no certain measures to prevent PCOS. PCOS does appear to run in families, suggesting a genetic role in its development.

See also [CONCEPTION](#); [CONTRACEPTION](#); EXERCISE AND HEALTH; [MENSTRUAL CYCLE](#); [OVA](#); [PREMATURE OVARIAN FAILURE \(POF\)](#); WEIGHT LOSS AND WEIGHT MANAGEMENT.

preeclampsia A complication of PREGNANCY in which a woman develops significant to severe HYPERTENSION (high BLOOD PRESSURE) and elevated protein in the URINE. Preeclampsia, sometimes called toxemia of pregnancy, is more common in a first pregnancy and in pregnant women who are under age 20 or over age 40 and in women who have DIABETES, kidney disease, or hypertension when they become pregnant. Preeclampsia also seems to run in families, suggesting a GENETIC PREDISPOSITION. For the most part, however, doctors do not know what causes preeclampsia to develop. In about 10 percent of women preeclampsia progresses to ECLAMPSIA, in which seizures occur and which is life-threatening for the woman and the FETUS she carries.

The primary symptoms of preeclampsia are

- edema (swelling due to fluid retention)
- NAUSEA and VOMITING
- disturbances of vision (blurred or double vision)
- ringing in the ears or other auditory disturbances

The elevation in blood pressure tends to occur as a surge, most commonly in the second and third trimesters. Most often the doctor detects preeclampsia in its early stages through regular PRENATAL CARE visits and monitoring. Prompt diagnosis and treatment with antihypertensive medications to lower blood pressure can often prevent complications from developing. The doctor may also recommend reduced activity or bedrest to help keep blood pressure down. CHILDBIRTH is the most effective treatment. When preeclampsia is moderate to severe and the pregnancy is 37 weeks or beyond, the doctor may induce labor or perform a CESAREAN SECTION (surgical childbirth). Many women who have preeclampsia are able to go through labor and delivery without additional risk to the fetus or themselves.

See also [GESTATIONAL DIABETES](#).

pregnancy The series of events, extending from CONCEPTION to delivery (CHILDBIRTH), through which a blastocyst (the clump of cells that implants in the endometrium, the lining of the UTERUS) becomes a baby. A full-term pregnancy spans 266 days. However, doctors calculate the estimated date of delivery, commonly called the due date, to be 280 days from the start of the last menstrual period.

Confirming Pregnancy

Though a missed menstrual period is the classic first sign of pregnancy, URINE pregnancy tests are now sensitive enough to detect minuscule amounts of pregnancy-related hormones in the urine only a few days after conception and well before the woman misses a period. Home pregnancy tests are generally as accurate as the tests health-care providers use, though following the directions precisely is important. False results are common because of mistakes such as using a urine sample other than the first of the day (which is

- HEADACHE

the most concentrated) or not properly timing the duration of the test. Most health-care providers will do a pregnancy BLOOD test at the first prenatal visit to confirm the pregnancy. Pregnancy tests, urine or blood, measure the presence of human chorionic gonadotropin (hCG) or beta hCG.

Early signs of pregnancy a woman may detect include

- tender, swollen breasts
- unexplained nausea and vomiting
- aversions to or cravings for certain foods, including smells and sights of them
- profound tiredness
- sensation of lower abdominal bloating
- increased URINATION
- lightheadedness or dizziness

The health-care provider's examination also detects signs of pregnancy, including changes in the texture (by internal palpation) and appearance of the CERVIX and an enlarged, softened uterus. As pregnancy advances the uterus rises out of the pelvis and into the abdomen (beginning around 12 weeks). As part of the diagnostic process the provider uses terminology to identify how many pregnancies and how many deliveries the woman has had previous to the current pregnancy, designating them with the Latin words *gravida* and *para*. A woman who has been pregnant twice and delivered twice is a gravida 2 para 2, for example, and a woman who is pregnant for the first time is a primigravida nullipara or gravida 1 para 0.

Key Changes During Pregnancy

The woman's body undergoes profound changes during the course of pregnancy. Hundreds of hormones unique to pregnancy initiate and facilitate these changes, the most obvious of which are enlarged breasts and a steadily expanding belly. This biochemical flood is also responsible for the emotional swings that characterize early pregnancy. Nearly every body system modifies its functions in some fashion to support the pregnancy and the developing FETUS.

Uterus and abdomen The woman's uterus, pelvis, and abdominal structures flex and expand to accommodate the fetus as it develops and

grows. The uterus, for example, can stretch up to 10 times its normal size during pregnancy. The numerous hormones unique to pregnancy act on connective tissue throughout the woman's body to soften ligaments and muscles, providing the pliability necessary to allow this expansion. This softening also accounts for the MUSCLE and JOINT aches, especially in the hips and knees, common in the last months of pregnancy.

The endometrium (lining of the uterus) remains spongy and vascular to support the PLACENTA. A plug of mucus collects in the cervix, helping block BACTERIA from entering the uterus. The tissues of the VAGINA and VULVA engorge with blood, softening in preparation for childbirth. As the pregnancy approaches term, the cervix softens and thins (effaces). With the contractions of labor the cervix dilates and the vagina expands to allow passage of the fetus.

Breasts Changes in the breasts, notably tenderness and swelling, are often the earliest indications of pregnancy as the breasts respond to the hormones. As pregnancy progresses a woman's breasts greatly enlarge and change in preparation for BREASTFEEDING (lactation) after birth. The mammary glands and ducts (milk glands and ducts) swell and around the seventh month begin producing colostrum, a fatty premilk that conveys important NUTRIENTS and antibodies for basic immunity to the infant.

Cardiovascular A woman's blood volume and cardiac output progressively increase as pregnancy advances. The heart enlarges somewhat, HEART RATE goes up, and blood pressure rises. In very early pregnancy the blood vessels dilate in anticipation of the increased blood volume, sometimes resulting in episodes of lightheadedness or dizziness. Some women also get vascular headaches in response to the changes taking place within the muscular walls of the arteries.

Gastrointestinal One of pregnancy's early hallmarks is MORNING SICKNESS, nausea and vomiting doctors believe results from the hormones that surge into the woman's blood circulation when the blastocyst implants. These same hormones are responsible for softening connective tissue and have similar actions on the muscular tissues of the gastrointestinal system, sometimes slowing peristalsis (movement of the intestines) enough to

cause CONSTIPATION. Drinking plenty of fluids, eating foods high in fiber, and walking for at least 30 minutes every day help keep the gastrointestinal system functioning at its best.

In the later months of pregnancy the enlarged uterus displaces the organs of the upper abdomen further upward against the DIAPHRAGM, pressuring the stomach to cause DYSPEPSIA (upset stomach and heartburn) and gastric reflux. These discomforts go away after the baby is born and the abdominal organs return to their normal positions.

Weight gain Weight gain is both normal and essential to support the pregnancy. Appropriate weight gain for a woman who is of healthy weight at the onset of pregnancy is 25 to 35 pounds; in OBESITY less weight gain, 15 to 25 pounds, is healthier for both mother and baby. About 15 to 18 pounds of the weight comes from the baby and organs that support it (uterus, placenta, AMNIOTIC FLUID). The changes in the breasts add 2 to 3 pounds; additional fluids (such as blood) and increased body fat account for the remainder. The most rapid weight gain typically occurs in the second trimester, 2 to 4 pounds per month.

Most women require only an additional 200 to 300 calories a day to meet their increased energy needs. Nutritious EATING HABITS are especially important to meet nutritional needs for vitamins and minerals. Pregnant women should take prenatal vitamins to make sure they receive adequate amounts of vital nutrients. Folic acid (folate) is

particularly crucial for proper development of the BRAIN and SPINAL CORD. Supplemental iron boosts the ability of the woman's blood to carry oxygen, helping prevent ANEMIA.

Health Care During Pregnancy

Though pregnancy is a natural event, not a medical condition, routine PRENATAL CARE provides optimal circumstances for the health of the woman and of the fetus. Current medical knowledge and technology make possible high-risk pregnancies as well as early intervention to avert or manage medical complications that may arise in the woman or the fetus. Screening tests and procedures can detect congenital and genetic abnormalities (BIRTH DEFECTS) that may require special medical attention during or after birth.

For further discussion of pregnancy within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also [ABORTION](#); [ADOPTION](#); [ECTOPIC PREGNANCY](#); [FAMILY PLANNING](#); [FERTILITY](#); [GESTATIONAL SURROGACY](#); [OVA](#); [PREMATURE BIRTH](#); [STILLBIRTH](#); [ZYGOTE](#).

premature ovarian failure (POF) A health condition in which a woman's OVARIES stop functioning before age 40. POF is a leading cause of INFERTILITY in women. Though POF causes MENOPAUSE-like symptoms and people (including doctors) sometimes refer to it as premature menopause, women

THE WOMAN'S BODY THROUGH PREGNANCY

Gestational Week	Body Characteristics
4 to 6	UTERUS soft and enlarged; breasts tender and swollen
12	belly begins to bulge; 2 to 4 pounds weight gain
16	darkened nipples and areola; dark line down center of abdomen
20	top of uterus at the level of the belly button; pregnancy obvious; breasts enlarged
24	Braxton-Hicks contractions; top of uterus above belly button; VULVA enlarged due to blood engorgement
28	weight gain of about 1 pound a week; minor swelling of the ankles and feet; size of uterus pressures BLADDER and DIAPHRAGM
32	breasts begin to leak colostrum; fetal movements visible through the abdominal wall
36	top of uterus near the bottom of the sternum; CERVIX begins to soften and thin (efface); pelvic ligaments and muscles soften and stretch
40	Strong Braxton-Hicks contractions; uterus completely fills the abdominal cavity; cervix continues to efface and begins to dilate; breasts engorged and frequently leak colostrum; mucous plug dislodges from cervix; water breaks (amniotic membrane ruptures)

who have POF often have irregular menstrual cycles for years after the onset of POF symptoms and do retain the ability to conceive, whereas menstrual cycles completely cease with menopause, ending the potential for pregnancy.

The reasons for POF are unclear though likely are a mix of genetic, hormonal, and perhaps autoimmune factors. Women who have POF have lower than normal levels of ESTROGENS and higher than normal FOLLICLE-STIMULATING HORMONE (FSH) levels in the BLOOD circulation, suggesting depletion or dysfunction of the ovarian follicles. Doctors do not know whether the abnormal HORMONE levels cause or result from follicular factors. CHROMOSOMAL DISORDERS such as TURNER'S SYNDROME and GENETIC DISORDERS such as ACHONDROPLASIA (a form of SKELETAL DYSPLASIA, often called dwarfism) also are associated with POF.

Symptoms and Diagnostic Path

The symptoms of POF are similar to those of menopause and commonly include

- HOT FLASHES and night sweats
- vaginal dryness and irritation (nonbacterial VAGINITIS)
- painful SEXUAL INTERCOURSE (dyspareunia)
- diminished LIBIDO
- low energy or fatigue
- irritability and mood swings
- irregular menstrual periods

The diagnostic path begins with a comprehensive medical examination, including PELVIC EXAMINATION, and blood tests to measure blood hormone levels (usually including a PREGNANCY test). The doctor may desire genetic tests as well, such as a KARYOTYPE, to evaluate the possibility of a genetic or chromosomal disorder. Women who have very mild Turner's syndrome may first learn of this diagnosis during evaluation for POF, as other symptoms of the syndrome may be so nominal as to escape detection.

Treatment Options and Outlook

Treatment with estrogen and progestin supplementation until closer to the age for natural menopause may relieve many POF symptoms

though does not usually improve FERTILITY. However, pregnancy remains possible and is something a woman should consider when her menstrual period does not occur as expected when she is taking hormone supplementation.

Women who have POF have increased risk for OSTEOPOROSIS and CARDIOVASCULAR DISEASE (CVD), and should follow lifestyle practices to support BONE and cardiovascular health. Such practices include calcium supplementation, daily physical exercise such as walking or running for cardiovascular health, resistance activities such as lifting weights to maintain MUSCLE mass and BONE DENSITY, nutritious EATING HABITS, and weight management. ASSISTED REPRODUCTIVE TECHNOLOGY (ART) methods using donor OVA (eggs) may provide pregnancy for a woman who has POF and desires to conceive.

Risk Factors and Preventive Measures

Known risk factors for POF are chromosomal or genetic disorders affecting the sex chromosomes or features of sexual development and ADDISON'S DISEASE (an autoimmune disorder affecting the ADRENAL GLANDS). Medical treatments such as CHEMOTHERAPY and RADIATION THERAPY may cause secondary POF. There are no known measures to prevent POF.

See also AUTOIMMUNE DISORDERS; POLYCYSTIC OVARY SYNDROME (PCOS); SEX CHROMOSOME; WEIGHT LOSS AND WEIGHT MANAGEMENT.

premature birth The delivery of an infant before 37 weeks gestational age, also called preterm birth. Though viability is possible after 24 weeks, many fetal organ systems do not reach maturity sufficient for independent life until near full term. Sometimes there are warning signs of premature birth that allow the doctor to attempt to delay CHILDBIRTH by administering medications to stop uterine contractions. The doctor may also help the FETUS prepare for independent life. Giving the mother injections of betamethasone, a corticosteroid, accelerates the fetus's lung development.

Though premature birth does not present any unusual risk for the woman, it often results in mild to moderate health challenges for the infant. Very early premature birth, between 24 and 32 weeks, presents grave health risks for the infant, who commonly requires extensive medical care

for several weeks to several months, depending on the gestational age at birth. About 10 percent of babies in the United States are born prematurely. The most common causes of premature birth are multiple PREGNANCY and PREECLAMPSIA. Women who have DIABETES, HYPERTENSION (high BLOOD PRESSURE), and chronic kidney disease have increased risk for premature delivery.

See also ABORTION; NEONATAL JAUNDICE; STILLBIRTH.

premenstrual syndrome (PMS) A constellation of symptoms that occurs in a regular pattern aligned with a woman's MENSTRUAL CYCLE. Doctors believe PMS results from the hormonal shift in the balance between ESTROGENS and PROGESTERONE that follows involution of the corpus luteum. This shift sets in motion the events that produce MENSTRUATION. PMS tends to begin during the last half of the luteal phase and continue to the onset of menstrual bleeding, typically spanning five to seven days. As many as 85 percent of women experience some symptoms of PMS; about 10 percent experience symptoms significant enough to interfere with daily activities. Some doctors call debilitating symptoms premenstrual dysphoric disorder (PMDD).

Symptoms and Diagnostic Path

The symptoms of PMS may vary from month to month in a woman and also vary widely among women. Common PMS symptoms include

- irritability, extreme emotions, and mood swings
- MASTALGIA (painful breasts)
- confusion, forgetfulness, and difficulty concentrating
- abdominal cramping and bloating
- low back ache or PAIN
- fluid retention and swelling of the hands, ankles, and feet
- weight gain (as much as two to four pounds)

The diagnostic path begins with a comprehensive medical examination, including PELVIC EXAMINATION. The doctor may ask the woman to keep a daily diary of her symptoms over three to six months, which helps to establish a clear pattern of symptoms and their severity. The doctor may

request BLOOD tests and abdominal ULTRASOUND to rule out hormonal imbalances, ovarian conditions, and other possible causes for symptoms.

Treatment Options and Outlook

Mild to moderate PMS often improves with lifestyle modifications, including sufficient sleep, nutritious EATING HABITS, daily physical exercise, MEDITATION or other relaxation methods, and reduced CAFFEINE consumption (though some women find the diuretic and mild stimulant effects of caffeine helpful). BIOFEEDBACK and ACUPUNCTURE are also often effective. Supplementation with B vitamins, vitamin E, and calcium appear to reduce PMS symptoms, though it may take several months for the effect to become apparent. Evening primrose oil, SOY and other PHYTOESTROGENS, DONG QUAI, and BLACK COHOSH are among the herbal remedies that may relieve PMS symptoms. Over-the-counter (OTC) NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) relieve HEADACHE and mastitis, and may reduce other symptoms because of their actions to suppress the release of PROSTAGLANDINS (chemicals that increase the sensitivity of nerves to pain signals).

Selective serotonin reuptake inhibitors (SSRIs), a class of ANTIDEPRESSANT MEDICATIONS, are effective in relieving moderate to severe PMS symptoms and are the current standard of care for PMS as well as PMDD. Researchers believe SSRIs work so well because they influence the neurohormonal interactions that take place in the BRAIN. Though some women find their symptoms improve with oral contraceptives (birth control pills), recent research suggests progesterone (which appears in the synthetic form progestin in many oral contraceptive formulas) is a key factor in causing PMS. Current clinical guidelines recommend oral contraceptives as treatment for PMS only when the woman also desires to take them as a means of preventing PREGNANCY.

Risk Factors and Preventive Measures

PMS occurs only in menstruating women. However, though PMS is very common not all menstruating women experience it. Some research suggests that women may metabolize progesterone differently, accounting for differences in its effects during the menstrual cycle. Lifestyle meas-

ures, medications, or a combination of approaches can help mitigate symptoms for many women, though there are no methods for preventing PMS.

See also [DYSMENORRHEA](#); MEDICINAL HERBS AND BOTANICALS; [MENOPAUSE](#).

prenatal care Routine and preventive health care provided during PREGNANCY to safeguard the health and well-being of the woman and the FETUS. In the United States routine prenatal care consists of regular visits to the health-care provider (family practitioner, obstetrician, or nurse midwife), URINE and BLOOD tests, BLOOD PRESSURE checks, and additional diagnostic procedures as needed such as ULTRASOUND, AMNIOCENTESIS, or CHORIONIC VILLI SAMPLING (CVS). The schedule of visits varies according to the trimester of pregnancy and any specific concerns about the pregnancy.

Ideally, prenatal care begins before CONCEPTION with a focus on nutritious EATING HABITS, healthy weight, appropriate management of any health conditions (such as DIABETES, HYPERTHYROIDISM, and HYPERTENSION), and abstinence from cigarette smoking, ALCOHOL consumption, and substance abuse. The prospective father should share this focus, as the health of both parents contributes to FERTILITY and fetal health. Also ideally, a woman who is planning pregnancy already receives routine medical examinations, including PELVIC EXAMINATION and PAP TEST, according to the recommendations appropriate for her age, sexual activity, and health history. Lifestyle habits to maintain the health of the woman and the fetus remain significant for the duration of pregnancy.

Health experts strongly encourage all women of childbearing age, regardless of their intentions toward pregnancy, to take a folic acid supplement. Folic acid, also called folate, significantly reduces the risk for serious BIRTH DEFECTS called NEURAL TUBE DEFECTS. However, the neural tube (the rudimentary CENTRAL NERVOUS SYSTEM) develops very early, well before a woman suspects she might be pregnant. Taking 400 micrograms (mcg) of folic acid supplement daily provides protection even when pregnancy is unexpected (as is the case with half of pregnancies that occur in the United States) and provides nutritional benefit for the woman. Oral contraceptives (birth control pills) deplete folic acid.

Prenatal Care: First Trimester

Routine prenatal care visits occur monthly during the first trimester, which extends through the 12th week of pregnancy. The first prenatal visit is more extensive than subsequent visits because the health-care provider conducts a comprehensive medical examination, including pelvic exam, and collects detailed information about the woman's health history, including any previous pregnancies, SEXUALLY TRANSMITTED DISEASES (STDs), childhood diseases, and immunizations. At the first prenatal visit the health-care provider also establishes a baseline of vital data such as height, weight, blood pressure, and size of the pelvic opening and the UTERUS. Routine blood tests done on the first prenatal visit commonly check BLOOD TYPE including Rh factor, ANEMIA, and antibodies for MUMPS, MEASLES, CHICKENPOX, HEPATITIS B, RUBELLA, and SYPHILIS. The provider may also recommend a blood test for HIV/AIDS and screening of both parents for cystic fibrosis if not yet done.

Another priority on the first prenatal visit is estimation of the anticipated due date for birth, which is important to assess whether the pregnancy and fetal growth are progressing as they should. Adding seven days and subtracting three months from the date the last menstrual period started gives the approximate due date, which the provider compares to findings from the pelvic examination to assess the age of the fetus.

At each subsequent prenatal visit during the first trimester the health-care provider tests a urine sample for GLUCOSE and protein, obtains weight and blood pressure, and measures the growth of the uterus. Pelvic exams are not usually necessary. If there are concerns about GENETIC DISORDERS or CHROMOSOMAL DISORDERS the provider may offer CVS (chorionic villi sampling) between the 10th and 12th weeks. At the last visit of the first trimester the health-care provider is often able to detect the fetal heartbeat using Doppler ultrasound.

Prenatal Care: Second Trimester

Routine prenatal visits continue monthly during the second trimester, the 13th through the 26th weeks of pregnancy. The growth of the uterus is more apparent and measurements of it more precise, allowing the health-care provider to refine

the prospective due date. Weight, blood pressure, and urine sample for glucose and protein remain staples of prenatal visits in the second trimester.

Around the 18th week the health-care provider offers a set of screening blood tests, the triple screen or the quad screen. These tests measure certain hormones and proteins in the woman's blood that may suggest neural tube defects such as SPINA BIFIDA and chromosomal disorders such as DOWN SYNDROME. The results of these tests are specific to the gestational age so the provider will be as certain as possible about the due date before conducting them.

It is important for the woman, her partner, and the provider to discuss the implications of positive results from screening tests, and for the woman and her partner to consider what actions they might take. The provider typically recommends amniocentesis to further evaluate positive triple screen or quad screen results. The provider may recommend abdominal ultrasound around the 20th week if the due date is questionable or if there is reason to suspect abnormalities in fetal development. At the end of the second trimester the provider typically requests a glucose challenge test to check for GESTATIONAL DIABETES as well as blood tests to check for anemia.

MATERNAL SCREENING BLOOD TESTS

Triple Screen

ALPHA FETOPROTEIN (AFP)
beta human chorionic gonadotropin (beta-HCG)
unconjugated estriol (uE3)

Quad Screen

AFP
beta-HCG
uE3
pregnancy-associated plasma protein A (PAPP-A)

Prenatal Care: Third Trimester

Routine prenatal care visits shift to every two weeks between 28 and 36 weeks and weekly from 36 weeks until delivery. The health-care provider continues to check weight, urine, and blood pressure. Early in the third trimester the provider discusses the potential for delivery by CESAREAN SECTION if the fetus is in a breech position or there are other circumstances that might increase the

risk to the fetus or the woman with a vaginal delivery.

At the 34th or 35th week the provider cultures swabbed samples from the VAGINA and rectum for group B streptococcus (GBS) BACTERIA, which some women harbor without harm to themselves but that can cause life-threatening INFECTION in the newborn. Women who test positive for GBS receive ANTIBIOTIC MEDICATIONS when they go into labor. The provider also monitors the status of GENITAL HERPES, when this STD is present, to be prepared for cesarean section should an outbreak occur near the anticipated time of delivery.

See also CONGENITAL ANOMALY; FAMILY PLANNING; FETAL ALCOHOL SYNDROME; PREVENTIVE HEALTH CARE AND IMMUNIZATIONS.

priapism A condition in which a man's PENIS remains erect for longer than four hours. Priapism is involuntary (not a function of sexual stimulation), painful, and requires immediate medical attention to prevent permanent damage to the penis and preserve sexual function. Priapism is most often a SIDE EFFECT of medication, notably medications to treat ERECTILE DYSFUNCTION and the antidepressant medication trazodone. It also may occur as a complication of SICKLE CELL DISEASE, GENITAL TRAUMA, and PROSTATE CANCER. Treatment may include evacuation of BLOOD from the corpora cavernosa, the tubular channels within the penis that fill with blood to establish an erection, via needle and syringe or intravenous catheter. The doctor may also inject the penis with vasoconstrictor medications. If medical interventions fail, surgery may be necessary to implant a shunt that allows blood to drain from the penis.

See also ANTIDEPRESSANT MEDICATIONS; PARAPHIMOSIS; PEYRONIE'S DISEASE.

prostate cancer A malignant (cancerous) tumor that arises from the glandular tissue of the PROSTATE GLAND, a walnut-size structure that encircles a man's URETHRA at the base of the BLADDER. Prostate cancer is one of the HORMONE-DRIVEN CANCERS that appears to have some genetic foundations as it tends to run in families. Prostate cancer also strongly correlates to increased age; it is rare among men under age 50 and affects more than half of men over age 70.

Prostate cancer is the most frequently diagnosed cancer among men in the United States and is primarily found in men over age 60. Though prostate cancer may take an aggressive path with widespread METASTASIS that leads to premature death, prostate cancer more often than not is a slow-growing cancer and runs a course that doctors can control through various treatments. Far more men die *with* prostate cancer than *from* prostate cancer. With early detection and treatment, prostate cancer may be curable.

The symptoms of prostate cancer are often difficult to distinguish from the symptoms of non-cancerous conditions that affect the prostate gland, particularly BENIGN PROSTATIC HYPERPLASIA (BPH). All men eventually develop some degree of BPH as they grow older, enlargement of the prostate gland begins to occur as a natural dimension of aging. However, BPH is not and does not become prostate cancer, though a man may have both conditions concurrently.

Symptoms and Diagnostic Path

Early to moderately advanced prostate cancer may cause no symptoms, with diagnosis resulting from further investigation of an abnormally high PROSTATE-SPECIFIC ANTIGEN (PSA) BLOOD level or abnormal findings during DIGITAL RECTAL EXAMINATION (DRE) performed during a ROUTINE MEDICAL EXAMINATION. When symptoms are present they may include

- frequent URINATION, particularly at night (NOC-TURIA)
- incomplete emptying of the bladder with urination, sometimes resulting in URINARY URGENCY, URINARY FREQUENCY, and URINARY TRACT INFECTION (UTI)
- reduced urinary flow, urinary hesitation (difficulty starting the flow of urine), and dribbling (difficulty stopping the flow of URINE)
- blood in the urine (HEMATURIA) OR SEMEN (hematospermia)
- sensation of heaviness or fullness in the lower abdomen (pelvic area)
- low BACK PAIN or rectal pressure

The diagnostic path may include DRE to palpate the prostate gland, blood tests to measure PSA levels and detect the presence of other TUMOR MARKERS, urinalysis, transrectal ULTRASOUND (TRUS), and biopsy (multiple tissue samples) of the prostate gland.

STAGING AND GRADING OF CANCER are critical for identifying and selecting the most appropriate treatment options. Several systems exist for cancer staging and grading. Because prostate cancer cells typically invade different areas of the prostate gland at varying levels of what pathologists call architectural disorder—the extent to which the cell structure deviates from normal—conventional staging and grading methods often cannot accurately classify the prostate cancer overall. Some areas of invasion may be fairly advanced and others minimally involved. The Gleason system and the Jewett system are methods unique to prostate cancer and the ones most doctors use to guide treatment decisions. In addition, conventional staging methods provide further classification.

Gleason pattern and score The Gleason system allows the pathologist to select the pattern (sometimes called grade) of the two most predominant architectures (primary and secondary) among the biopsy samples and combine them into a score that represents the character of the prostate cancer overall. There are five patterns and nine scores possible within the Gleason system. The lower the Gleason score (also called the Gleason sum), the more likely the cancer is confined and will respond to treatment. However, the patterns that establish the score are also important. For example, a prostate cancer that has a Gleason score of 7 coming from 3 + 4 has a more positive prognosis than one with a Gleason score of 7 coming from a 4 + 3 because the first number indicates the primary pattern and pattern 3 is less aggressive than pattern 4. It is important to know both patterns as well as the score.

Jewett staging system The Jewett system, also called the Jewett-Whitmore system, assigns four alphabetic values to the extent of cancer metastasis, with numeric subvalues for more precise classification.

Conventional staging Some doctors additionally use conventional staging and grading systems

GLEASON PATTERNS AND SCORES FOR PROSTATE CANCER

Gleason Pattern

pattern 1	cells and architecture nearly normal (well differentiated)
pattern 2	cells nearly normal though glandular cells beginning to invade MUSCLE tissue within the PROSTATE GLAND
pattern 3	cells still maintain glandular structure though invasion of muscle tissue within the prostate gland is significant; possible regional METASTASIS
pattern 4	significant cell abnormality with loss of normal architecture and distorted glandular structure; probable regional metastasis; possible distant metastasis
pattern 5	cells and architecture completely irregular and abnormal (undifferentiated); probable distant and multiple metastases

Gleason Score

2	lowest possible score; very early cancer with excellent prognosis
3 to 4	slow growing tumor; early cancer with good prognosis
5 to 6	mildly aggressive tumor likely confined to the prostate gland
7	moderately aggressive tumor with possible regional metastasis
8 to 9	aggressive tumor with regional metastasis
10	highly aggressive tumor with multiple distant metastases

JEWETT STAGING SYSTEM CLASSIFICATIONS

stage A	very early, localized cancer; only indication is elevated BLOOD PROSTATE-SPECIFIC ANTIGEN (PSA) level A1: well-differentiated or single site within PROSTATE GLAND A2: clearly abnormal cells or multiple sites within prostate gland
stage B	localized cancer palpable via DIGITAL RECTAL EXAMINATION (DRE); may cause mild symptoms B1: single site B2: multiple sites
stage C	METASTASIS to adjacent tissue but not to LYMPH nodes C1: tumor is outside the prostate gland but nonobstructive C2: tumor obstructs the BLADDER or the URETHRA (urinary symptoms)
stage D	metastasis to lymph nodes or distant organs D1: regional LYMPH NODE involvement D2: distant lymph node or organ involvement (including BONE) D3: RECURRENCE after treatment

to further classify and understand the prostate cancer’s characteristics to optimally tailor treatment approaches. The two main conventional staging systems are

- the numeric system, which identifies five levels of tumor aggressiveness (stage 0 through stage 4, or IV)
- the American Joint Committee on Cancer (AJCC) tumor, node, and metastasis (TNM) system, which assigns numeric values to the size

of the tumor, invasion of LYMPH nodes, and spread to distant organs or structures

Treatment Options and Outlook

The treatment of choice for men under age 70 is nearly always PROSTATECTOMY, a surgical OPERATION to remove the prostate gland, with adjuvant (follow-up) CHEMOTHERAPY, RADIATION THERAPY, or HORMONE THERAPY as appropriate. Radiation therapy is most effective when the cancer remains confined to the prostate gland. For men over age 70, in

whom prostate cancer is likely to be slow growing and remain localized, the doctor may recommend less invasive approaches such as diligent monitoring (watchful waiting) or radiation therapy (external beam or internal seeding).

No matter his age at the time of diagnosis, a man must consider the many factors that contribute to the relative benefits and risks of treatment options for his stage and grade of cancer, prognosis, other health conditions, and personal desires. Treatments such as surgery and hormone therapy may affect sexual function and have other undesirable side effects. It is important to fully understand the potential implications of treatment options and their effects on *QUALITY OF LIFE*. Though prostate cancer is the second-leading cause of cancer deaths among men in the United States (*LUNG CANCER* being first), treatment provides long-term management and prostate cancer is not fatal in the majority of men who develop it.

Risk Factors and Preventive Measures

The most significant risk for prostate cancer is age. Prostate cancer is uncommon in men under age 50 though is present in about half of men over age 80. Other factors that increase the risk for prostate cancer are African American heritage and long-term *EATING HABITS* that feature foods high in saturated fat. There is some evidence that dietary consumption of soy proteins, such as in soybean-based foods and in nutritional supplement products, and *LYCOPENE*, found in tomatoes and pink grapefruit, improve the ability of prostate glandular cells to resist cancerous changes. The medicinal botanical product *SAW PALMETTO*, available in the United States as a nutritional supplement, may help maintain overall *PROSTATE HEALTH*.

Health experts differ in their opinions about the value of routine screening procedures, such as *DRE* and *PSA* blood levels, for detecting prostate cancer and especially for improving the outcome of treatment. *PSA* in particular tends to generate a high percentage of false-positive findings, thrusting men into more invasive diagnostic procedures that have increased risks as well as heightened emotional stress. However, both *DRE* and *PSA* are components of a routine medical examination in

the United States for men over age 50. It is important for a man and his doctor to carefully and comprehensively evaluate all aspects of the man's personal prostate health and to weigh the risks and benefits of further diagnostic assessment.

See also *CANCER TREATMENT OPTIONS AND DECISIONS*; *CARCINOMA*; *DIET AND HEALTH*; *LIFESTYLE AND HEALTH*; *MEDICINAL HERBS AND BOTANICALS*; *SURGERY BENEFIT AND RISK ASSESSMENT*.

prostate gland The gland in the male reproductive tract that produces most of the volume of *SEMEN*. About the shape and size of a walnut, the prostate gland wraps around the *URETHRA* at the neck of the *BLADDER*. The back of the prostate gland rests against the front wall of the *RECTUM*. A tough, fibrous membrane forms a single capsule enclosing the 30 to 50 clusters of glandular tissue that make up the prostate gland. There are three distinct structures of glandular tissue, which urologists refer to as zones—peripheral, transition, and central—though how the zones differ in function remains unknown. The prostate gland also contains nonglandular cells, primarily *MUSCLE* and connective tissue cells that help move prostatic secretions into the urethra.

Prostate gland cells produce their secretions under stimulation by *TESTOSTERONE*, which reaches them through the *BLOOD* circulation. The seminal vesicles, which lie just behind the prostate gland, store mature *SPERM* encased in a thick, jellylike solution that prevents them from motility. During *ORGASM* and *EJACULATION*, the seminal vesicles and the prostate gland each contract, mixing sperm and prostatic fluid in the urethra to form semen. The prostatic fluid contains an enzyme, *PROSTATE-SPECIFIC ANTIGEN (PSA)*, that thins the semen to allow the sperm to become motile. Ejaculation then carries the semen through the urethra and out the tip of the *PENIS*.

As a man ages the prostate gland slowly enlarges, a condition called *BENIGN PROSTATIC HYPERPLASIA (BPH)*. In most men *BPH* remains innocuous, causing no symptoms or even awareness of its presence. Other health conditions that can affect the prostate gland are *PROSTATITIS (INFLAMMATION OR INFECTION)* and *PROSTATE CANCER*. The surgical *OPERATION* to remove the prostate gland is

PROSTATECTOMY. The doctor can palpate (feel) the prostate gland through the wall of the rectum during DIGITAL RECTAL EXAMINATION (DRE), which helps detect prostate enlargement as well as abnormalities that suggest other health concerns affecting the prostate gland. Because the risk for prostate cancer increases after age 40, DRE palpation of the prostate gland becomes part of the ROUTINE MEDICAL EXAMINATION for men age 40 and older.

HEALTH CONDITIONS THAT
CAN AFFECT THE PROSTATE GLAND

bacterial PROSTATITIS	BENIGN PROSTATIC HYPERPLASIA (BPH)
nonbacterial prostatitis	prostadynia
PROSTATE CANCER	prostatic ABSCESS

See also AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; CANCER PREVENTION.

prostate health Measures a man can take throughout his life to maintain healthy function of his PROSTATE GLAND. The prostate gland, which wraps around the URETHRA at the base of the BLADDER, produces the primary volume of SEMEN, the fluid that carries SPERM out of the body during EJACULATION, and the enzyme PROSTATE-SPECIFIC ANTIGEN (PSA), which thins the semen to permit sperm motility. The prostate gland functions unobtrusively through most of a man's life. In early to mid-adulthood the most significant risk to prostate health is INFECTION (PROSTATITIS), which may be due to the spread of a sexually transmitted disease (STD) such as GONORRHEA or may result from non-STD causes.

In late midlife and beyond the prostate gland begins to slowly enlarge, a natural aspect of aging. Doctors call the enlargement BENIGN PROSTATIC HYPERPLASIA (BPH). For about half of men over age 60 BPH becomes significant enough to constrict or obstruct the urethra (the tubelike structure that drains URINE from the bladder), causing symptoms of urinary obstruction such as URINARY FREQUENCY and hesitation. With increasing age the risk for PROSTATE CANCER, the most serious health condition affecting the prostate gland, also increases.

Dietary and lifestyle measures may slow the progression of both BPH and prostate cancer. Foods that support prostate health include

- SOY (soybeans, soy protein, tofu, tempeh)
- tomatoes and tomato-based foods such as tomato sauce and tomato paste, which contain LYCOPENE
- pink grapefruit and watermelon, which also contain lycopene
- cruciferous vegetables (broccoli, cauliflower, cabbage, kale), which contain sulforaphane and other isothiocyanates, substances that appear to help prostate gland cells fight cancer

A number of studies show the herbal remedy SAW PALMETTO can improve the symptoms of mild to moderate BPH, apparently by shrinking the prostate gland tissues. Some studies show a correlation between high BODY MASS INDEX (BMI) and more aggressive prostate cancers, and other studies demonstrate a lower risk for cancer overall (as well as CARDIOVASCULAR DISEASE and DIABETES) with healthy body weight and regular physical exercise. In the United States, preventive health-care recommendations call for PSA BLOOD level measurements and DIGITAL RECTAL EXAMINATION (DRE) as part of a man's ROUTINE MEDICAL EXAMINATION beginning around age 50. These tests may detect abnormal function or size of the prostate gland that could be early indications of BPH or prostate cancer.

See also AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; CANCER PREVENTION; DIET AND HEALTH; EXERCISE AND HEALTH; LIFESTYLE AND HEALTH; PREVENTIVE HEALTH CARE AND IMMUNIZATIONS; SEXUAL HEALTH; URETHRITIS; WEIGHT LOSS AND WEIGHT MANAGEMENT.

prostatectomy A surgical OPERATION to remove part or all of the PROSTATE GLAND. The prostate gland encircles the URETHRA at the base of the BLADDER. It produces the fluid that mixes with SPERM to form SEMEN and produces the enzyme PROSTATE-SPECIFIC ANTIGEN (PSA), which facilitates sperm motility after EJACULATION. Prostatectomy is primarily treatment for PROSTATE CANCER and BENIGN PROSTATIC HYPERPLASIA (BPH) that constricts the urethra to the extent that it interferes with URINATION. Removal of the prostate gland ends a man's FERTILITY though not necessarily his ability to have and ERECTION and ORGASM.

Surgical Procedure

Surgeons may choose from a number of operations to remove the prostate gland. The choice depends on the reason for the operation, the size of the prostate gland, and the man's overall health status. There are six commonly performed prostatectomy operations: transurethral retrograde prostatectomy (TURP), transurethral incision of the prostate (TUIP), three open prostatectomy operations (suprapubic, retropubic, and perineal), and radical open prostatectomy.

Transurethral retrograde prostatectomy (TURP)

TURP has long been the standard, and remains the most common, surgical operation to remove obstructive prostate gland tissue due to BPH (non-cancerous prostate gland enlargement) when the prostate gland remains relatively small. The surgeon uses an endoscopic instrument called a resecting cystoscope or resectoscope, inserted through the PENIS and urethra to the prostate gland.

The surgeon passes a cutting tool through the resectoscope to make an incision through the urethra and remove part or all of the prostate gland by shaving away layers of tissue. After removing the prostate gland the surgeon sutures the urethra back to the neck of the bladder. The removed shreds of tissue collect in the bladder and pass out with the URINE over the first few days after surgery. TURP generally requires three days in the hospital and two to four weeks recovery time until full return to normal activities. A man who has had a TURP usually retains erectile function though has RETROGRADE EJACULATION (ejaculation into the bladder).

Transurethral incision of the prostate (TUIP)

TUIP is a cystoscopic procedure in which the surgeon makes a series of small incisions through the urethra into the prostate gland. The incisions relieve the pressure the enlarged prostate gland is exerting against the urethra, without removing prostate tissue, restoring the free flow of urine. TUIP is treatment only for noncancerous prostate enlargement, such as BPH, and is used only in limited circumstances that depend on the size and structure of the prostate gland. TUIP is often an AMBULATORY SURGERY procedure (a same-day surgery) with full return to normal activities in three to five days. Erectile and ejaculatory functions nearly always remain normal.

Open prostatectomy The three operations of open prostatectomy, sometimes called simple prostatectomy, involve making an incision through the surface of the SKIN to reach the prostate gland. The incision for suprapubic or retropubic prostatectomy extends from the navel (belly button). In the suprapubic approach the surgeon reaches the prostate gland through the bladder. In the retropubic approach the surgeon reaches the prostate gland without entering the bladder. The incision for perineal prostatectomy is between the SCROTUM and the ANUS. Open prostatectomy removes the prostate gland and seminal vesicles intact. The surgeon may also remove nearby LYMPH nodes (lymphadenectomy) when the operation is to treat prostate cancer.

Open prostatectomy is major surgery that requires a stay of up to eight days in the hospital and six to eight weeks recovery (sometimes longer) before return to regular daily activities. There is moderate risk for significant complications such as bleeding, URINARY INCONTINENCE, and damage to the nerves that supply the penis resulting in ERECTILE DYSFUNCTION.

Radical prostatectomy Radical prostatectomy is a treatment for prostate cancer in which the surgeon removes the prostate gland, seminal vesicles, and surrounding tissue (fat, MUSCLE, and connective tissue) during an operation that can take five hours or longer. Often the surgeon removes adjacent lymph nodes as well. Radical prostatectomy is major surgery that requires about 10 days in the hospital and up to four months for recovery. Radical prostatectomy is treatment for prostate cancer and has a high risk for complications such as urinary incontinence and erectile dysfunction, though these complications may improve over time.

In some circumstances the surgeon may opt to perform radical prostatectomy laparoscopically, inserting a laparoscope and surgical instruments through several small incisions in the abdomen. The laparoscopic approach significantly lessens the risk for complications and shortens recovery time, though the operation is nonetheless major surgery. Sometimes the surgeon may use laparoscopic surgery to remove pelvic lymph nodes while using the open perineal approach to remove the prostate gland.

Risks and Complications

Prostatectomy, particularly an open or radical approach, is extensive surgery with potential complications that require careful consideration. Among them are excessive bleeding during or after surgery that may necessitate BLOOD TRANSFUSION, INFECTION, retrograde ejaculation, urinary incontinence, bladder damage, rectal damage, and erectile dysfunction. Generalized risks include reaction to ANESTHESIA and blood clots. The risk for complications depends on the reason for the prostatectomy (cancer or noncancerous condition), the type of operation, age, and overall health status. Surgeons prescribe prophylactic antibiotics to help prevent infection and antiemolism therapies such as ANTICOAGULATION THERAPY and compression stockings or boots to help prevent blood clots.

Outlook and Lifestyle Modifications

For many men, prostatectomy ends the symptoms of the condition that necessitated the operation. Because the prostate gland continues to slowly enlarge as a man ages, about 20 percent of men who have TURP to treat BPH find their symptoms return in 10 to 15 years, requiring additional treatment. Many men are able to return to normal activities, including sexual activities, within a few months of their surgeries. However, prostate cancer may require adjuvant (follow-up or accompanying) treatment after surgery.

See also ANTIBIOTIC PROPHYLAXIS; CANCER TREATMENT OPTIONS AND DECISIONS; SURGERY BENEFIT AND RISK ASSESSMENT.

prostate-specific antigen (PSA) An enzyme PROSTATE GLAND cells produce. Prostatic fluid, the cumulative secretions of prostate gland cells, contains high levels of PSA. PSA acts on the jellylike substance that encases SPERM during their storage in the seminal vesicles, liquefying the substance when the sperm mix with prostatic fluid in the URETHRA during EJACULATION. This action restores motility to the sperm.

Measuring the BLOOD concentration of PSA provides information about the health status of the prostate gland. In the healthy prostate gland of a man under age 40, the prostate gland cells form a tight structure that directs nearly all PSA the cells

produce into the prostatic fluid; only a small amount of PSA escapes to circulate in the blood. In certain health conditions, most notably PROSTATE CANCER, PSA blood levels rise. Prostate cancer disrupts the structure and organization of prostate gland cells, allowing much higher concentrations of PSA to enter the blood circulation. Other health conditions such as PROSTATITIS, BENIGN PROSTATIC HYPERPLASIA (BPH), and even URINARY TRACT INFECTION (UTI) can also cause PSA levels to rise.

As well, PSA also normally rises with increasing age because the prostate gland slowly enlarges beginning around age 40, a process that also alters the structure and organization of prostate gland cells. Because of this natural change, normal PSA blood values differ according to a man's age. Blood PSA concentrations above the value for age may suggest the presence of prostate disease, including prostate cancer. In general, a blood PSA level of 4 nanograms per milliliter (ng/mL) may indicate the need for further evaluation of the prostate gland's health.

NORMAL VALUES FOR BLOOD PROSTATE-SPECIFIC ANTIGEN (PSA) LEVELS

Age	PSA Blood Concentration
40 to 49	< 2.5 nanograms per milliliter (ng/mL)
50 to 59	< 3.5 ng/mL
60 to 69	< 4.5 ng/mL
70 to 79	< 6.5 ng/mL

However, health experts disagree about the value of blood PSA levels for prostate cancer screening and detection. There is limited consensus around what the values mean, there are several methods for measuring PSA that are not equivalent to one another, and there is a higher rate of false-positive PSA results—PSA levels that are elevated for reasons other than prostate disease—than many doctors find acceptable. These factors are of concern because the next step of diagnosis, biopsy, is invasive and carries risk for numerous complications. Many doctors find PSA blood tests more useful when treating disorders of the prostate gland, such as BPH and prostate cancer, as measures to help assess the effectiveness of treatment.

See also AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; CANCER PREVENTION.

prostatitis INFLAMMATION, INFECTION, OR PAIN of the PROSTATE GLAND. Prostatitis may be acute (come on suddenly) or chronic (persist or recur over time). Urologists classify five types of prostatitis:

- Acute bacterial prostatitis occurs as a result of infection with BACTERIA, usually URINARY TRACT INFECTION (UTI), that infiltrates the prostate gland. SEXUALLY TRANSMITTED DISEASES (STDs), notably GONORRHEA and CHLAMYDIA, may also cause acute bacterial prostatitis. Treatment with appropriate ANTIBIOTIC MEDICATIONS usually cures the infection.
- Chronic bacterial prostatitis occurs as a result of an underlying chronic health condition that allows continued or repeated bacterial access to the prostate gland. Treatment requires long-term, and sometimes repeated, antibiotic therapy as well as efforts to resolve the underlying condition.
- Chronic inflammatory prostatitis causes pain and exists when there is inflammation but no infection. Treatment is with NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs) to reduce inflammation and relieve pain.
- Asymptomatic inflammatory prostatitis does not cause any symptoms and is sometimes a factor in male INFERTILITY that shows up during FERTILITY testing. NSAIDs may improve the inflammation.
- Prostatodynia, also called chronic noninflammatory prostatitis, involves neither inflammation nor infection though pain is persistent and sometimes debilitating. Doctors do not know what causes prostatodynia. Medications such as alpha blockers, used to treat BENIGN PROSTATIC HYPERPLASIA (BPH), and NSAIDs sometimes provide relief. BIOFEEDBACK, ACUPUNCTURE, and prostatic massage are other methods to relieve pain.

Symptoms and Diagnostic Path

The primary symptom of all but asymptomatic inflammatory prostatitis is pain in the lower pelvis. Men who have acute bacterial infection often have FEVER and feel quite ill. Men who have chronic bacterial prostatitis may feel intermittently fatigued. The diagnostic path for prostatitis may

include DIGITAL RECTAL EXAMINATION (DRE) to palpate the prostate gland, measurement of BLOOD PROSTATE-SPECIFIC ANTIGEN (PSA) levels, urinalysis including urine culture, and SEMEN analysis to look for the presence of red blood cells (evidence of bleeding), white blood cells (evidence of inflammation), and bacteria (evidence of infection). When symptoms are chronic, additional diagnostic procedures may include transrectal ULTRASOUND (TRUS), COMPUTED TOMOGRAPHY (CT) SCAN, prostate biopsy, or CYSTOSCOPY.

Treatment Options and Outlook

Treatment and outlook depend on the identified underlying cause for the symptoms. Because the structure of the glandular tissue within the prostate gland is such that it prevents blood components from entering the prostate gland (a protective mechanism to prevent ANTIBODY formation and to keep the semen PSA concentration high), the course of antibiotic therapy for bacterial prostatitis is lengthy, typically four to eight weeks. A complication of untreated or undertreated bacterial prostatitis is prostatic ABSCESS (the formation of a contained pocket of pus), which may require a cystoscopic procedure under ANESTHESIA to drain the abscess.

Risk Factors and Preventive Measures

Prompt diagnosis and treatment of UTIs and STDs significantly reduce the risk for bacterial prostatitis. There are no clear preventive measures for other forms of prostatitis.

See also CHRONIC PAIN; CYSTITIS; MALDYNIA; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; URETHRITIS.

puberty The transition from childhood to the sexual and reproductive maturity that marks adulthood. Puberty occurs under the influence of hormonal shifts. The path of puberty tends to start and end about two years earlier for girls than for boys. Puberty in most industrialized parts of the world begins between ages 10 to 15 and concludes between ages 17 to 19. SECONDARY SEXUAL CHARACTERISTICS emerge during puberty, coinciding with ADOLESCENCE, the emotional and psychologic changes that occur during the shift from childhood to adulthood.

Puberty begins with hormonal changes the HYPOTHALAMUS and the PITUITARY GLAND initiate that stimulate the gonads (ovaries in women and testicles in men) to begin producing gonadotropins (sex hormones)—ESTROGENS and ANDROGENS. The PINEAL GLAND, which regulates the body's circadian rhythms, also appears to play a role. Researchers do not know what triggers these changes. Because external factors such as nutritional status and illness can influence the timing of puberty, researchers suspect body mass (height and weight) may somehow signal the endocrine system. CHROMOSOMAL DISORDERS involving the sex chromosomes, such as TURNER'S SYNDROME, which affects girls, and KLINEFELTER'S SYNDROME, which affects boys, alter or prevent natural puberty.

In both sexes, the first indication of puberty is the growth of HAIR under the arms and around the GENITALIA. At first the hair is light and fine; as puberty progresses the hair darkens and thickens. Hair on the legs also darkens and becomes more dense. There is usually an accompanying growth spurt, which in boys particularly may amount to six inches or more of height within a year. Boys begin to broaden at the shoulders and girls at the hips during this surge of growth. The remaining changes that occur with puberty are gender specific.

Puberty in Girls

BREAST buds, firm bumps that form beneath the nipples, mark the onset of estrogen-driven changes occurring in the girl's body. In most girls breast budding occurs simultaneously with the development of pubic and axillary hair though one set of events may precede the other. Over the course of one to three years the breasts continue to grow and take form and the girl's body takes on a womanly appearance. Generally, about the time the pattern of body hair becomes adult-like the girl begins to menstruate, indicating her ovaries are mature and functional. Puberty concludes in girls when the MENSTRUAL CYCLE is regular and predictable. External factors that can influence the start of MENSTRUATION (MENARCHE) include OBESITY, which tends to cause earlier menarche, and intense physical activity such as athletic competition, which tends to cause later menarche. Both are within the range of normal.

Puberty in Boys

Enlargement of the SCROTUM and testicles marks the onset of TESTOSTERONE-driven changes occurring in the boy's body. The boy's voice lowers in register and deepens. Growth continues at a rapid rate. Over the course of one to three years the PENIS thickens and elongates, and the testicles begin producing SPERM. Sexually stimulated ERECTION and NOCTURNAL EMISSION ("wet dreams") are common. Toward the conclusion of puberty hair on the arms may also become darker, longer, and more dense, and hair begins to grow on the chest. Puberty concludes in boys when the genitalia reach adult proportions, which occurs at age 15 to 19.

Precocious Puberty

Occasionally disturbances of hormonal function may result in early, or precocious, puberty, which doctors define as the onset of puberty before age 8 in girls and age 9 in boys. Treatment for precocious puberty depends on the underlying cause of the hormonal disturbance when the doctor can identify it; a common cause is pituitary ADENOMA (noncancerous tumor in the pituitary gland). Often the cause remains unknown (idiopathic precocious puberty), in which case the doctor may administer GONADOTROPIN-RELEASING HORMONE (GNRH) to regulate the pituitary gland's release of LUTEINIZING HORMONE (LH), the hormone that stimulates estrogen and testosterone. There are usually no adverse effects of idiopathic precocious puberty.

See also AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; HYPOGONADISM.

retrograde ejaculation A circumstance in which a man's SEMEN enters the BLADDER instead of ejecting from the PENIS during EJACULATION. Semen and URINE share the URETHRA for their exit from a man's body. A tiny valve in the urethra at the neck of the bladder ordinarily closes across the entry to the bladder during ejaculation, directing the flow of semen through the penis. When this valve does not close, semen takes the path of least resistance and enters the bladder during ejaculation. A man may notice retrograde ejaculation as a "dry ORGASM" in which very little discharge leaves the penis with orgasm. Retrograde ejaculation does not present any health concerns for the man

though results in INFERTILITY when all semen enters the bladder. Analysis of the first urine after ejaculation shows the presence of SPERM. That first urine after ejaculation may also appear cloudy.

BENIGN PROSTATIC HYPERPLASIA (BPH), a non-cancerous enlargement of the PROSTATE GLAND, is the most common cause of retrograde ejaculation. The prostate gland surrounds the neck of the bladder; in BPH the gland may compress the urethra in such a way as to prevent the valve from properly functioning. Surgery to treat BPH or PROSTATE CANCER may permanently damage or remove the

valve. Retrograde ejaculation may also occur in men who have DIABETES, particularly when BLOOD GLUCOSE (sugar) regulation is poor. Some medications that affect smooth MUSCLE function may also cause retrograde ejaculation. When the cause is a medication SIDE EFFECT, ejaculation returns to normal when the man stops taking the medication. When the cause is a health condition such as BPH or diabetes, retrograde ejaculation is likely not reversible.

See also [FERTILITY](#); [PROSTATE HEALTH](#); [SEXUAL HEALTH](#); [URINARY TRACT INFECTION \(UTI\)](#).

scrotum The saclike structure, a thin layer of **MUSCLE** and **SKIN**, suspended from the base of a man's pelvis that contains the **TESTICLES**. A pair of ligaments, the spermatic cords, extend from the lower abdomen to support the scrotum. The spermatic cords also serve as the conduits for the **BLOOD** vessels and nerves that supply the testicles. The abdominal and scrotal muscles contract or relax to raise or lower the scrotum, maintaining the appropriate temperature for spermatogenesis (**SPERM** production). Sperm production, which is a key function of the testicles, requires a temperature of 96°F to 96.5°F, about 2 degrees lower than body temperature. Pubic **HAIR** covers the outside of the scrotum after **PUBERTY**.

See also **HERNIA**; **SPERMATOCELE**; **VARICOCELE**.

secondary sexual characteristics The physical changes that distinguish the genders from each other. Secondary sexual characteristics emerge with **PUBERTY** and establish sexual and reproductive maturity: males produce viable **SPERM** capable of causing **PREGNANCY**, and females produce ripened **OVA** (eggs) capable of fertilization that results in pregnancy.

FEMALE SECONDARY SEXUAL CHARACTERISTICS

growth of pubic and axillary (underarm) **HAIR**
thickened and coarse or dark leg hair
enlarged breasts and broadened hips

MALE SECONDARY SEXUAL CHARACTERISTICS

growth of pubic, axillary, chest and facial hair
thickened, darkened, and coarse arm and leg hair
broadened shoulders and chest
increased **MUSCLE** mass and definition
deepened voice and prominent Adam's apple in the **THROAT**
enlarged **TESTICLES**, enlarged and elongated **PENIS**

See also **CONCEPTION**; **CONTRACEPTION**; **FERTILITY**; **MENSTRUAL CYCLE**; **MENSTRUATION**; **PREGNANCY**.

semen The fluid of a man's **EJACULATION**. In a fertile man about 5 percent of the semen content is **SPERM**; in a man who has had a **VASECTOMY** semen does not contain sperm. The seminal vesicles and the **PROSTATE GLAND** produce the milky fluid of semen, which is primarily a water base that contains proteins, sugars (notably fructose and some **GLUCOSE**), lipids (fatty acids), electrolytes, and **PROSTAGLANDINS**. The bulbourethral glands, also called Cowper's glands, add a gelatinous secretion to the semen that thickens it. Semen may flow back into the **BLADDER** rather than out of the **PENIS** (**RETROGRADE EJACULATION**) in a man with a **PROSTATECTOMY** (surgery to remove the prostate gland).

The electrolytes protect sperm on their journey through the **VAGINA** and into the **UTERUS**. The sugars, particularly fructose, and lipids provide nutrition for the sperm. Vaginal secretions are highly acidic and deadly to sperm. The thickness of semen helps contain and insulate sperm as they travel through the **VAGINA**, though the semen thins by the time it reaches the **UTERUS** to release the sperm. The electrolytes in semen make it highly alkaline, helping neutralize the vaginal environment to improve sperm survival. Prostaglandins help suppress the **IMMUNE RESPONSE**, the natural reaction of the woman's **IMMUNE SYSTEM** to the presence of the sperm. The semen also has the ability to carry various pathogens such as viruses and **BACTERIA** that can spread **SEXUALLY TRANSMITTED DISEASES** (**STDs**).

Semen analysis is a laboratory examination of a semen sample to measure the concentrations of its ingredients and the number and characteristics of the sperm. **ALCOHOL** consumption, cigarette smok-

ing, and frequency of ejaculation are among the factors that influence the volume and content of semen.

SEMEN NORMAL VALUES PER EJACULATION

semen volume	1.5 to 6.5 milliliters
sperm count	20 to 250 million per milliliter
pH	7.1 to 8.0
fructose	30 milligrams per milliliter

See also [CONTRACEPTION](#); [HEMATOSPERMIA](#); [HYDROCELE](#); [PATHOGEN](#); [SEXUAL INTERCOURSE](#); [SEXUALLY TRANSMITTED DISEASE \(STD\) PREVENTION](#); [VARICOCELE](#); [VIRUS](#).

sexual dysfunction Physical or psychologic circumstances that interfere with sexual interest or sexual activity. Most people experience some degree of sexual dysfunction over the course of their lifetimes. The causes of sexual dysfunction are numerous; most are transient (improve or go away with time). Physical illness, injury, surgery, disability, medication side effects, emotional stress, job pressures, [CHILDBIRTH](#) and [PARENTING](#) responsibilities, [GRIEF](#), [DEPRESSION](#), and relationship discord are among the most common factors. People who have experienced [SEXUAL ASSAULT](#) or rape, in childhood or as adults, may also have difficulty establishing or maintaining healthy sexual relationships. As well, an individual's attitudes toward and understanding of sex affect the nature and quality of sexual interaction.

Painful [SEXUAL INTERCOURSE](#), called [DYSpareunia](#), is the most common form of physical sexual dysfunction in women. [Dyspareunia](#) may result from insufficient vaginal lubrication (which becomes more common after [MENOPAUSE](#)), vaginal muscle spasms ([VAGINISMUS](#)), inflammation or irritation of the [VAGINA](#) ([VAGINITIS](#)) or [VULVA](#) ([vulvitis](#)), pain in the external [GENITALIA](#) ([VULVODYNIA](#)), [UTERINE PROLAPSE](#), [ENDOMETRIOSIS](#), [UTERINE FIBROIDS](#), or perineal injury (such as perineal tear or [EPISIOTOMY](#) repair). Chronic [PELVIC INFLAMMATORY DISEASE \(PID\)](#) may also cause pain during sex. Psychologic or emotional factors may also contribute to [dyspareunia](#).

The most common form of physical sexual dysfunction in men is the inability to achieve or maintain an [ERECTION](#) ([ERECTILE DYSFUNCTION](#)), which may result from physical or psychologic factors. [ATHEROSCLEROSIS](#) (accumulation of plaque

deposits in the arteries that narrows the channel for [BLOOD FLOW](#)), [DIABETES](#), peripheral [NEUROPATHY](#) (damage to the small nerves that supply the penis), long-term cigarette smoking, and medication side effects are the leading physical causes of erectile dysfunction in men. Men may also experience pain with intercourse as a consequence of [URETHRITIS](#), [PEYRONIE'S DISEASE](#), and inadequate lubrication during penetration.

Excessive [ALCOHOL](#) use, [ILlicit DRUG USE](#), and heavy or long-term cigarette smoking contribute to sexual dysfunction in men and women. Alcohol and many drugs, prescription or "street," depress [LIBIDO](#). Alcohol affects the health of blood vessels and nerves; long-term alcohol abuse is another cause of erectile dysfunction in men. Cigarette smoking also affects blood flow; [NICOTINE](#) is a powerful vasoconstrictor (narrows blood vessels) and the changes in blood oxygen levels that occur when smoking affect the function of cells throughout the body. These effects are most significant for [NERVE](#) cells, which require consistent levels of oxygen.

Symptoms and Diagnostic Path

The primary symptom of sexual dysfunction is the reduced ability to engage in or enjoy sexual activity. Men and women may experience difficulty achieving [ORGASM](#) (sexual climax); this is more common in women. Psychologic and emotional symptoms of sexual dysfunction in men or women may include diminished [libido](#) (sex drive), disinterest in sex, or excessive interest in sex. The diagnostic path begins with a comprehensive medical examination, including [PELVIC EXAMINATION](#) for women, and discussion about factors that might be contributing to the symptoms. The doctor may perform additional diagnostic procedures, depending on the findings of the medical examination, such as blood tests (men and women), cultures of vaginal fluids (women) or any discharges (men and women), or [pelvic ULTRASOUND](#) (women).

Treatment Options and Outlook

Treatment options depend on the identified causes of the symptoms. Treatment may be as straightforward as changing or stopping a medication that is causing the symptoms or treating an underlying physical condition. Often the symptoms of sexual

dysfunction resolve when the factors responsible for them go away, such as when a person changes from a high-pressure job to one that has a lower level of stress. Sometimes simply the process of discussing life circumstances in response to the doctor's questioning provides a connection between the circumstances and the symptoms that the person had not been able to see.

Sexual dysfunction can be a complex intertwining of physical and psychologic factors that benefits from a combination of treatment for the physical conditions and therapy (counseling) for the psychologic and emotional factors. Relationship or personal therapy may help a person come to insight and understanding about his or her attitudes and expectations about sex.

Risk Factors and Preventive Measures

The key risk factors for sexual dysfunction are physical or psychologic conditions or emotional issues that affect interest in and satisfaction with sexual activity. Appropriate treatment combined with open and compassionate communication can help partners address their concerns and achieve a level of sexual interaction that accommodates each partner's needs. Though it is not always possible to prevent health and life circumstances from resulting in sexual dysfunction, most causes of sexual dysfunction are treatable.

See also ALCOHOLISM; EJACULATION; FERTILITY; INFERTILITY; PARAPHIMOSIS; PELVIC INFLAMMATORY DISEASE (PID); PHIMOSIS; PRIAPISM; RETROGRADE EJACULATION; SEXUAL HEALTH.

sexual health Measures men and women can take to experience sexuality in ways that support their physical and emotional well-being. A key factor for sexual health is overall health—nutritional EATING HABITS, daily physical exercise, MEDITATION or relaxation, adequate sleep, and adequate time for leisure or recreational activities. Sexual health further incorporates measures to reduce the risk for health conditions specifically related to sexual activity such as INFECTION with SEXUALLY TRANSMITTED DISEASES (STDs) and undesired PREGNANCY (CONTRACEPTION).

In addition to the physical factors of sexual health are the psychologic, emotional, and social factors. Despite the tendency of health-care

providers to focus on physical concerns such as STDs because of the health issues these infections entail, the emotional intimacy of sexual relationships is an essential component of sexual health. It is sometimes difficult to determine when a relationship is consenting and when it is abusive. Sexual health requires mutual appreciation for each partner's needs, physical and emotional.

Young people especially may face pressure to enter into sexual relationships yet are uncertain that they are ready or willing to do so. The consequences may be far reaching. One million teens become pregnant in the United States each year. STDs such as GENITAL HERPES, HEPATITIS B, and hepatitis C are treatable but not curable. Though treatment regimens now greatly extend life and improve quality of life, HIV/AIDS remains ultimately fatal. Other STDs may cause scarring and other damage that results in permanent INFERTILITY.

See also BREAST HEALTH; BREAST SELF-EXAMINATION (BSE); PROSTATE HEALTH; SEXUAL ASSAULT; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; TESTICULAR SELF-EXAMINATION (TSE).

sexual intercourse Sexual activity that involves penetration between sexual partners. In conventional context sexual intercourse is the insertion of a man's erect PENIS into a woman's VAGINA and is the primary mechanism of human reproduction. Male EJACULATION propels SEMEN into the vagina, where the SPERM it contains may unite with an egg (ovum) if the woman is ovulating and conditions are conducive. In contemporary context the term more broadly encompasses vaginal sex, anal sex, and oral sex between partners of either gender as acts of intimacy and pleasure, physical and emotional, that may or may not include the intent to conceive a PREGNANCY.

See also CONCEPTION; CONTRACEPTION; ORGASM; OVULATION; SEXUAL ASSAULT; SEXUAL HEALTH; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION.

sexually transmitted diseases (STDs) Infections that spread from one person to another during sexual activity, causing illness or damage to the body. The pathogens that cause STDs may be BACTERIA, viruses, or parasites. STDs, also called sexually transmitted infections (STIs), are significant concerns worldwide, diminishing overall health

and QUALITY OF LIFE. STDs infect tens of millions of people in the United States and hundreds of millions of people throughout the world.

STDs may not have symptoms though the person continues to be infectious (capable of passing the STD to sex partners). Often a person has more than one STD at the same time, a circumstance called co-infection. It is possible for reinfection with the same STD to occur after treatment. ANTIBIOTIC MEDICATIONS are the mainstay of treatment for bacterial STDs. ANTIVIRAL MEDICATIONS may alleviate symptoms in viral STDs such as GENITAL HERPES and lessen the risk for transmitting the VIRUS to others, though the virus often remains in the body and symptoms recur.

Though all STDs are treatable, many are not curable. Some, such as HEPATITIS B and HUMAN PAPILLOMAVIRUS (HPV), are known causes of cancer (LIVER CANCER and CERVICAL CANCER, respectively). Hepatitis C may be fatal and at present HIV/AIDS is always fatal, though treatment and supportive lifestyle measures can manage both conditions for years to decades. STDs are a leading cause of PELVIC INFLAMMATORY DISEASE (PID) in women, a serious INFECTION that can result in INFERTILITY by causing scarring and occlusion (blockage) of the FALLOPIAN TUBES and sometimes the CERVIX.

Oral contraceptives (birth control pills), intrauterine devices (IUDs), cervical diaphragms, spermicides, VASECTOMY, TUBAL LIGATION, and HYSTERECTOMY, though effective methods of CONTRACEPTION, do not prevent INFECTION with SEXUALLY TRANSMITTED DISEASES (STDs).

Abstinence (no sexual partners) is the most effective means to prevent infection with STDs. Among people who are sexually active, key measures to reduce the risk for STD infection are

- long-term, mutual monogamy (one exclusive sex partner)
- male latex condom use with every sexual act (vaginal intercourse, anal intercourse, oral sex, partner MASTURBATION)

The effectiveness of these measures varies for the specific STD. Latex condoms are highly effective

for preventing GONORRHEA and HPV, for example, though may be less effective for protecting against genital herpes and HIV/AIDS. The female condom is another barrier method of CONTRACEPTION that provides some, but more limited, protection from STD infection compared to the male condom. Unprotected contact with bodily fluids (pre-ejaculate or vaginal secretions), such as may occur during heavy petting and foreplay, carries the same risk for STD infection as does actual intercourse.

Infections not typically characterized as STDs, such as TUBERCULOSIS, may also pass between people during sexual activity. Conversely, some infections characteristically transmitted through sexual contact may also pass via other means such as shared needles among intravenous DRUG users (notably HIV/AIDS and hepatitis). An infant may acquire gonorrhea, CHLAMYDIA, and genital herpes during CHILDBIRTH (passage through the VAGINA). An infant may also acquire congenital herpes without passing through the birth canal if the mother first becomes infected when she is pregnant.

Because many STDs are highly contagious and prompt treatment can minimize their spread as well as prevent long-term health complications for infected individuals, health experts strongly encourage diagnostic testing and treatment for all sexual partners of everyone who acquires an STD. In the United States, community health centers and public health services provide low-cost or free STD testing and treatment. Private doctors and other health-care providers also diagnose and treat STDs.

See also ANTIBIOTIC RESISTANCE; [SEXUAL HEALTH](#); SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION.

sperm The male cells of reproduction, also called gametes. A spermatozoon (single sperm cell) is a haploid cell; it contains one half of the genetic material necessary for human life. The epididymis within the testicle (also called the testis) produces sperm, a process called spermatogenesis, at the rate of hundreds of millions each day from PUBERTY (the onset of sexual maturity) through the end of life. The tissues of the TESTICLES absorb sperm that remain in the epididymis for longer than six weeks, allowing the supply of sperm to remain fresh.

Spermatogenesis The production of new sperm cells begins with the division and differentiation of

SEXUALLY TRANSMITTED DISEASES (STDs)

STD	Cause	Symptoms	Treatment and Outlook
CHLAMYDIA	BACTERIA: <i>Chlamydia trachomatis</i>	often no symptoms; men may have discharge from PENIS and burning with URINATION; women may have vaginal discharge	treatable and curable with antibiotic medications
GENITAL HERPES	VIRUS: HERPES SIMPLEX 2 (HSV-2)	burning, itching, chancrelike sores; vaginal discharge in women; burning with urination in men	not curable but symptom relief with ANTIVIRAL MEDICATIONS
GONORRHEA	bacteria: <i>Neisseria gonorrhoeae</i>	often no symptoms; burning with urination and discharge from the penis in men; vaginal discharge in women	treatable and curable with antibiotic medications though some strains are resistant
HEPATITIS B	virus: hepatitis B virus (HBV)	JAUNDICE, FEVER, NAUSEA, VOMITING, swollen and tender LIVER	preventable with hepatitis B VACCINE postexposure prophylaxis
hepatitis C	virus: hepatitis C virus (HCV)	jaundice, fever, nausea, vomiting, swollen and tender liver	postexposure prophylaxis
HIV/AIDS	virus: human immunodeficiency virus (HIV)	flu-like symptoms when INFECTION occurs; typically no symptoms until AIDS emerges	not curable and ultimately fatal; antiretroviral drugs can keep the virus in check for delay of disease manifestation and remission of symptoms
HUMAN PAPILLOMAVIRUS (HPV)	virus: human papillomavirus (HPV)	often no symptoms; may cause genital warts	not curable though infection often runs its course in several years; various methods to remove warts; some strains associated with CERVICAL CANCER
nongonorrheal URETHRITIS	bacteria: various	burning with urination; discharge from the penis in men	treatable and curable with antibiotic medications
SYPHILIS	bacteria: <i>Treponema pallidum</i>	painless chancre that may be unnoticeable; SKIN RASH; fever; late stage symptoms often systemic	treatable and curable with antibiotic medications
TRICHOMONIASIS	PROTOZOA: <i>Trichomonas vaginalis</i>	foul-smelling, discolored discharge; painful urination in men; vaginal or vulvar itching or burning in women	treatable and curable with metronidazole

germ cells in the seminiferous tubules. Specialized cells called Sertoli cells nourish and protect the new sperm cells, ushering them into the epididymis where they grow to maturity as they migrate through the 10 to 12 feet of tightly coiled

tubule that makes up this testicular structure. Their journey takes sperm to the ejaculatory ducts, where they mix with SEMEN. A mature spermatozoon consists of a head (the cell body) containing genetic material and a whiplike tail that

provides mobility. ANDROGENS, notably TESTOSTERONE, and other hormones regulate spermatogenesis. Spermatogenesis is a continuous process.

Fertilization The role of the sperm is to fertilize the ovum (egg), the first step in establishing PREGNANCY. SEXUAL INTERCOURSE, in which the man's erect PENIS enters the woman's VAGINA, is the natural mechanism through which sperm gain access to the woman's reproductive tract. From 20 to 250 million sperm leave the testicles within the semen, the fluid that nourishes and protects the sperm, during each EJACULATION. The sperm swim through the fluids in the vagina, enter the UTERUS through the CERVIX, and continue to the entrance of the FALLOPIAN TUBES at the top of the uterus.

Of the millions of sperm that begin this journey, most die before reaching the fallopian tube. Surviving sperm continue through the fallopian tube; fertilization takes place if there is an ovum (egg) also in the fallopian tube and a sperm is able to penetrate its surface membrane. Multiple factors influence this ability, including the shape of the sperm head, the remaining motility of the sperm tail to thrust the head through the ovum's membrane, and the environment within the fallopian tube. Once a single sperm penetrates the shell of the ovum, the ovum closes itself to further penetration. Only the head of the sperm enters the ovum; the tail of the sperm drops off outside the ovum. Multiple pregnancies occur when two or more sperm simultaneously penetrate the ovum (identical multiples) or when two or more OVA are present in the fallopian tubes (fraternal multiples). Abnormalities of sperm structure or motility may interfere with the sperm's ability to reach or penetrate the ovum.

For further discussion of sperm within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also [ASSISTED REPRODUCTIVE TECHNOLOGY \(ART\)](#); CELL STRUCTURE AND FUNCTION; [FERTILITY](#); [INFERTILITY](#); SECONDARY SEXUAL CHARACTERISTICS; [SEXUAL HEALTH](#).

spermatocele A cyst containing dead SPERM that forms in the epididymis. Doctors do not know what causes spermatoceles, also called epididymal cysts, to develop though suspect they result from

some sort of obstruction that blocks their flow through the epididymis. A spermatocele is round, firm, and clearly defined. A man may discover a spermatocele during routine TESTICULAR SELF-EXAMINATION (TSE) or the doctor may find it during ROUTINE MEDICAL EXAMINATION. A large spermatocele may cause PAIN. ULTRASOUND of the SCROTUM confirms the diagnosis. No treatment is necessary for a small spermatocele that does not cause symptoms. For large spermatoceles or spermatoceles that cause pain, surgery to remove the spermatocele is the most effective treatment. However, surgery may impair FERTILITY because it usually involves removing a portion of the epididymis.

See also [HYDROCELE](#); [SURGERY BENEFIT AND RISK ASSESSMENT](#); [VARICOCELE](#).

sperm donation The collection of a man's SEMEN, which contains SPERM, for use in FERTILITY treatments. The man obtains the semen for donation through MASTURBATION to produce EJACULATION. Sperm banks (facilities that collect and store donated sperm) have varying policies for qualifying sperm donors. In general a sperm donor must be between the ages of 18 and 45, have no known genetic or hereditary conditions, and have no exposure to infectious diseases such as HIV/AIDS, HEPATITIS, and SEXUALLY TRANSMITTED DISEASES (STDs). Sperm donors have no legal rights or responsibilities for children conceived with their sperm and typically remain anonymous.

See also [ASSISTED REPRODUCTIVE TECHNOLOGY \(ART\)](#); [GESTATIONAL SURROGACY](#).

stillbirth The death of the FETUS after 24 weeks of gestation. There are numerous causes for stillbirth; often the reason remains unknown. Sometimes the obstetrician cannot detect the fetal heartbeat during a routine PRENATAL CARE visit; more often the woman notices the fetus has stopped moving. An ULTRASOUND can confirm the death, after which the doctor induces labor to deliver the baby. Death may also occur during CHILDBIRTH. The loss of a PREGNANCY through stillbirth is emotionally traumatic for parents, family members, and friends.

See also [ABORTION](#); [GRIEF](#); [PREMATURE BIRTH](#); [SUPPORT GROUPS](#).

testicles The paired male organs, also called the male gonads, that produce SPERM and ANDROGENS, notably TESTOSTERONE. Each egg-shaped testicle is about two inches long and an inch in diameter. A man’s testicles may be slightly different from each other in size. The testicles reside side by side in the SCROTUM, a saclike structure suspended outside the body from the lower pelvis. The testicles are outside the body because spermatogenesis (the generation, or production, of sperm) requires a temperature two to three degrees below normal body temperature. A hollow ligament, the spermatic cord, extends from the abdomen to the testicle through the inguinal canal, carrying the ARTERY, VEIN, LYMPH structures, and nerves that supply the testicle.

The outer layer of the testicle is the tunica albuginea, a sheath of fibrous tissue that contains and protects the structures within the testicle. Tightly coiled tubules, the seminiferous tubules and the epididymis, make up the main mass of the testicle. The cells that fill the space between the tubules are the Leydig cells, also called the interstitial cells, which produce testosterone. The seminiferous tubules contain germ cells, from which new sperm cells (spermatozoa) arise, and Sertoli cells, which nourish and support the developing sperm cells. The Sertoli cells draw testosterone into the seminiferous tubules, which sperm cells require to come to maturation, and prevent antibodies in the BLOOD from entering the seminiferous tubules.

As the sperm cells develop, they travel from the seminiferous tubules to the epididymis, another coiled tubule. The epididymis incubates spermatozoa to maturity during the 12 days or so it takes for them to journey through the convolutions of the epididymis, during which they acquire tails

and motility (the ability to move). The vas deferens then carries sperm from the epididymis to the ejaculatory duct, which is within the lower pelvis.

HEALTH CONDITIONS THAT CAN AFFECT THE TESTICLES

CRYPTORCHIDISM	EPIDIDYMITIS
GENITAL TRAUMA	HYDROCELE
HYPOGONADISM	INFERTILITY
KLINEFELTER’S SYNDROME	ORCHITIS
SPERMATOCELE	TESTICULAR CANCER
TESTICULAR TORSION	VARICOCELE

For further discussion of the testicles within the context of the structures and functions of reproduction and sexuality, please see the overview section “The Reproductive System.” For further discussion of the testicles within the context of the structures and functions of the endocrine, system please see the overview section “The Endocrine System.”

See also [CONCEPTION](#); [CONTRACEPTION](#); [ORCHIECTOMY](#); [ORCHIOPEXY](#); [PROSTATE GLAND](#); [SEXUAL HEALTH](#); [VAS DEFERENS](#); [VASECTOMY](#).

testicular cancer A malignant (cancerous) tumor that arises from the tissue of a man’s testicle. Testicular cancer is usually unilateral (occurs only in one testicle), though sometimes occurs bilaterally (in both TESTICLES), and is most common in early adulthood (ages 20 to 34). With detection before the cancer metastasizes (spreads elsewhere in the body), the cure rate for testicular cancer is 99 percent. Doctors in the United States diagnose testicular cancer in about 8,000 men each year.

The two main types of testicular cancer are seminoma and nonseminoma, though some testicular cancers contain a mix of these types. Oncologists classify mixed testicular cancer tumors as nonseminoma because the nonseminoma cells

tend to be dominant in determining the tumor’s behavior. The distinction is important because the types have different patterns of aggressiveness (rate and way in which the tumor grows), METASTASIS, and responsiveness to treatment.

Symptoms and Diagnostic Path

The most common symptom of testicular cancer is a painless though sometimes tender lump or swelling in the SCROTUM. The man may discover

the lump or swelling during TESTICULAR SELF-EXAMINATION (TSE) or coincidentally, or the doctor may find it during ROUTINE MEDICAL EXAMINATION. Testicular cancer also may cause few symptoms until it has grown and spread outside the testicle, such as to organs in the abdomen. In such circumstances, symptoms may be more generalized and include low pelvic or low back heaviness or pressure, fatigue, and overall sense of not feeling well (malaise).

BASIC STAGING OF TESTICULAR CANCER		
Stage	Meaning	Treatment Options
stage 0/carcinoma in situ	cancer remains contained in the cells of their origin	radical inguinal ORCHIECTOMY
stage 1	cancer remains confined to a local tumor in one testicle	radical inguinal orchiectomy seminoma: inguinal and retroperitoneal LYMPH NODE irradiation nonseminoma: retroperitoneal lymph node dissection or two cycles of chemotherapy
stage 2 nonbulky	cancer has spread to retroperitoneal LYMPH nodes and nodes are 2 inches or smaller	radical inguinal orchiectomy seminoma: inguinal and retroperitoneal lymph node irradiation nonseminoma: retroperitoneal lymph node dissection, then two cycles of chemotherapy
stage 2 bulky	cancer has spread to retroperitoneal lymph nodes and nodes are larger than 2 inches	radical inguinal orchiectomy seminoma: three cycles of chemotherapy nonseminoma: three or four cycles of chemotherapy
stage 3 nonbulky	cancer has spread to lymph nodes outside the abdomen and to the LUNGS though all metastasized tumors are ¾ inch or smaller	radical inguinal orchiectomy seminoma: three or four cycles of chemotherapy; RADIATION THERAPY for BRAIN METASTASIS nonseminoma: three or four cycles of chemotherapy; surgery to remove any remaining metastatic tumors
stage 3 bulky	cancer has spread to lymph nodes outside the abdomen and nonlung sites such as the LIVER or brain, and some metastasized tumors are larger than ¾ inch	radical inguinal orchiectomy seminoma: four cycles of chemotherapy; radiation therapy for brain metastasis nonseminoma: four cycles of chemotherapy; surgery to remove any remaining metastatic tumors clinical trials
stage 4/recurrent	cancer has returned after treatment	surgery for small, isolated metastases high-DOSE chemotherapy

The diagnostic path typically includes BLOOD tests to look for TUMOR MARKERS (proteins in the blood circulation that suggest the presence of cancer), such as ALPHA FETOPROTEIN (AFP) and lactate dehydrogenase (LDH), and ULTRASOUND of the scrotum, which may indicate whether the growth is fluid-filled (more likely a cyst or HYDROCELE) or solid (more likely a tumor).

Though biopsy (removal of a sample of the tumor's tissue for laboratory examination) is the means of establishing a cancer diagnosis in most other types of cancer, the risk that the biopsy will cause the release of cancer cells into the blood or LYMPH circulation is very high with testicular cancer because of the circulatory and lymphatic structures of the testicle. The urologist may consider biopsy when both testicles are involved or when a man has only one testicle. In such a circumstance the OPERATION begins as would an inguinal orchiectomy but the surgeon sends a tissue sample for the pathologist to examine and waits for the report of cancer or not cancer before proceeding. Otherwise laboratory analysis of the tumor occurs after removal of the testicle and its spermatic cord. The pathologist then identifies the type and stage of the cancer, which determines appropriate treatment options.

Treatment Options and Outlook

Surgery to remove the testicle containing the cancer is the first line of treatment. The operation of choice is radical inguinal ORCHIECTOMY, performed with the man under general ANESTHESIA. The surgeon makes an incision in the groin and pulls the testicle up from the scrotum to remove it, intact, along with its spermatic cord. The spermatic cord contains the blood and lymph vessels that supply the testicle; removing the entire testicular structure significantly reduces the risk for stray cancer cells entering the blood and lymph circulations to spread elsewhere in the body.

For seminomas or large tumors, the surgeon may also remove lymph nodes in the lower abdomen that are the path of lymph drainage from the spermatic cord (retroperitoneal LYMPH NODE dissection). Though a more extensive surgery, such an operation is very successful in preventing the spread of the cancer.

Most men then receive adjuvant (accompanying) treatment with RADIATION THERAPY or CHEMOTHERAPY, depending on the type and stage of the cancer. Tumors that contain only seminoma cells (pure seminoma) tend to stay contained longer and are very sensitive to radiation therapy. Tumors that contain nonseminoma cells tend to metastasize (spread) earlier and are more responsive to chemotherapy. Oncologists typically administer chemotherapy using combinations of drugs for several cycles (three or four) of treatment.

CHEMOTHERAPY AGENTS TO TREAT TESTICULAR CANCER

bleomycin	carboplatin
cisplatin	cyclophosphamide
etoposide	ifosfamide
vinblastine	

Testicular cancer is among the most treatable cancers. Testicular cancer detected and treated while it remains localized in one testicle (stage 0 or stage 1) has a current five-year survival rate of 99 percent; oncologists consider this a cure rate because the cancer rarely recurs. The RECURRENCE rate (likelihood for the cancer to return after treatment) is very low, though a man who has had testicular cancer has increased risk for cancer in the remaining testicle (usually a new cancer rather than a metastasis of the original cancer) or for other types of cancer.

Treatment for testicular cancer does not affect a man's sexuality though may affect his FERTILITY. Most people feel fatigued during cancer treatment, which often lowers LIBIDO (interest in sexual activity). However, most testicular cancer treatments do not affect a man's ability to obtain ERECTION, reach orgasm, or achieve EJACULATION. Extensive retroperitoneal lymph node dissection has a slight risk for NERVE damage that can result in RETROGRADE EJACULATION (in which SEMEN enters the BLADDER rather than exiting the PENIS during ejaculation). Many men retain fertility after testicular cancer, though doctors recommend sperm banking for men who may desire to father children because many factors influence fertility so it is not certain. A man may choose to have a testicular prosthesis implanted to restore the cosmetic appearance and feel of the scrotum.

Risk Factors and Preventive Measures

The most significant risk factor for testicular cancer is undescended testicle (CRYPTORCHIDISM), even after corrective treatment. Untreated cryptorchidism in which the testicle remains within the abdomen presents a very high risk as well as low potential for early detection of testicular cancer. Testicular atrophy, such as may occur after INFECTION WITH THE MUMPS VIRUS, BACTERIAL ORCHITIS, OR SEXUALLY TRANSMITTED DISEASES (STDs), and family or personal history of testicular cancer also increase a man's risk for testicular cancer. Though there are no measures to prevent testicular cancer, monthly TSE is an effective means of early detection. Regular follow-up care, including blood tests to measure tumor markers and imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN OR POSITRON EMISSION TOMOGRAPHY (PET) SCAN, is important.

See also [BREAST CANCER](#); CANCER TREATMENT OPTIONS AND DECISIONS; HORMONE-DRIVEN CANCERS; [PROSTATE CANCER](#); [SEXUAL HEALTH](#); STAGING AND GRADING OF CANCER; SURGERY FOR CANCER.

testicular self-examination A technique by which a man checks his TESTICLES for lumps, PAIN, and other abnormalities as a means of early detection of TESTICULAR CANCER and noncancerous conditions that may affect the testicles and a man's fertility, such as VARICOCELE and HYDROCELE. The primary purpose of TSE is to familiarize a man with the characteristics and anatomy of his testicles so he can detect changes that occur because it is these changes that may signal health conditions that require medical treatment. Though the main intent of TSE is early detection of testicular cancer, as mentioned, the technique also detects noncancerous conditions such as SPERMATOCELE, which can reduce fertility.

Health experts recommend TSE monthly, such as on the first day of every month, and suggest doing TSE in the shower when the SCROTUM is relaxed and lowered and the hands are soapy. TSE takes only a few minutes, following these steps:

1. Cup the testicles in one hand to support them.
2. Gently roll one testicle between the fingers, feeling for small lumps or unusual tenderness. The testicle should feel firm and smooth.

3. Use the fingers to feel the cordlike structure that runs from top to bottom, along the back of the testicle, the epididymis, exploring for hard lumps or areas of unusual tenderness. The epididymis is a tightly coiled structure that should feel somewhat lumpy or ropelike.
4. Use the fingers to feel the tubelike structure that runs from bottom to top along the side of the testicle, the VAS DEFERENS, checking for lumps or areas of unusual tenderness. The vas deferens should feel smooth and firm, and should move easily within the scrotum.
5. Repeat for the other testicle.

A doctor should promptly evaluate any changes or unusual findings such as lumps. It is normal for the testicles to be somewhat different in size and for one to hang lower than the other within the scrotum. Factors that increase a man's risk for developing testicular cancer include undescended testicle (CRYPTORCHISM), even after treatment to correct it, and family or personal history of testicular cancer. Testicular cancer is most common in men between the ages of 20 and 40, though can occur at any age. With early detection and treatment testicular cancer is highly treatable or curable, which is what makes TSE so important.

See also [BREAST SELF-EXAMINATION \(BSE\)](#); [PROSTATE HEALTH](#); [ROUTINE MEDICAL EXAMINATION](#); [SEXUAL HEALTH](#).

testicular torsion A condition in which the spermatic cord twists within the SCROTUM, turning the testicle and jeopardizing its BLOOD supply. Testicular torsion is very painful and can result in loss of the testicle due to strangulation (cutting off the flow of blood to the testicle). Testicular torsion may occur as a result of injury or may occur spontaneously (without apparent cause) and is most common in boys between the ages of 8 and 14. Normally connective tissues firmly attach the epididymis to the SCROTUM; in testicular torsion this attachment either did not exist (congenital) or broke free with exertion or a blow to the TESTICLES.

Testicular torsion is a medical emergency that requires urgent treatment from a doctor.

The key symptoms of testicular torsion are PAIN, swelling, and discoloration (cyanosis) of the scrotum. Symptoms usually appear suddenly, though some boys or men have recurring symptoms over time. Because of the structure of the spermatic cord, testicular torsion most often affects the left testicle. Chronic symptoms suggest congenital detachment of the epididymis from the scrotum. The diagnostic path includes careful physical assessment of the testicles, usually by a urologist. ULTRASOUND (usually Doppler ultrasound) can confirm the diagnosis.

Treatment, when diagnosis comes within six to eight hours of the first symptoms, is emergency surgery to restore the testicle to its normal position and attach it to the scrotum (ORCHIOPEXY). The testicle cannot survive more than six to eight hours after symptoms emerge; after this time necrosis (death of the tissue) sets in and the only treatment is to remove the testicle (ORCHIECTOMY). With rapid and appropriate treatment the urologist can save the testicle about 80 percent of the time. However, testicular atrophy (wasting) and necrosis (tissue death) remain possible for up to six months after the surgery to remedy testicular torsion.

The longer the time between the onset of symptoms and surgery, the greater the likelihood for impaired FERTILITY even when the urologist can save the testicle. This is because the SPERM that escape into the tissues of the testicle establish or activate the IMMUNE RESPONSE, which produces antibodies to the man's own sperm that then attack the sperm as the testicles produce them.

See also EPIDIDYMITIS; GENITAL TRAUMA; HERNIA; ORCHITIS; SEXUAL HEALTH.

tubal ligation A surgical OPERATION to sever (cut) or tie off a woman's FALLOPIAN TUBES to prevent PREGNANCY. Tubal ligation is a form of permanent CONTRACEPTION, sometimes called tying the tubes or sterilization. There are two fallopian tubes, one leading from each ovary to the UTERUS. Cutting or cauterizing the fallopian tubes prevents the union of OVA, which travel from the OVARIES to the uterus, and SPERM, which travel from the uterus toward the ovaries. This blocks fertilization and prevents pregnancy.

Surgical Procedure

The most common method of tubal ligation is an abdominal operation usually performed as a laparoscopic procedure in an AMBULATORY SURGICAL FACILITY (outpatient or same-day surgery). The doctor may also perform tubal ligation as an OPEN SURGERY at the conclusion of a scheduled CESAREAN SECTION, provided the woman has given informed consent for the procedure.

The woman first receives ANESTHESIA, which may be general anesthesia (deep sleep) or regional anesthesia such as an epidural block. The surgeon then makes a single incision (called a single puncture technique) or several small incisions near the area of the navel (belly button) to insert the laparoscope and operating instruments. The incisions give access to the fallopian tubes. The surgeon places surgical clips or uses cautery to close the tubes. There may or may not be SKIN sutures, depending on the method the surgeon uses. The operation typically takes 35 to 45 minutes.

The woman spends one to three hours in the recovery room after the operation, until she emerges from the effect of the anesthesia. Most women go home within four to six hours of the operation. There is some abdominal discomfort for one to three days, for which the doctor will prescribe or recommend appropriate ANALGESIC MEDICATIONS. Full recovery may take two to three weeks, though many women can return to most normal activities within a few days. INFERTILITY is immediate.

Risks and Complications

As with any surgery, tubal ligation carries the risk for excessive bleeding, INFECTION, and reaction to the anesthesia. However, these complications are uncommon. Also possible though uncommon is PELVIC INFLAMMATORY DISEASE (PID), in which infection becomes widespread within the fallopian tubes and uterus and may also involve other abdominal structures. Rarely a fallopian tube may spontaneously reanastomose (reconnect), resulting in unexpected fertility usually detected through pregnancy.

Complications that may occur months to years after the operation include abdominal adhesions (the formation of restrictive SCAR tissue within the abdominal cavity) and ECTOPIC PREGNANCY, a life-

threatening circumstance that typically occurs when a tube partially reanastomoses but the fertilized egg cannot pass through the tube to the uterus and instead begins to grow in the fallopian tube or the abdominal cavity.

Outlook and Lifestyle Modifications

Tubal ligation has no effect on a woman's LIBIDO (sex drive), and in fact may increase a woman's interest in sexual activity because she no longer worries about unintended pregnancy. However, tubal ligation does not protect against SEXUALLY TRANSMITTED DISEASES (STDs) or HIV/AIDS.

The intent of tubal ligation is to establish permanent infertility (sterility), and a woman should consider tubal ligation to be permanent though it is sometimes possible to reverse a tubal ligation through a second surgery. The operation to reverse tubal ligation is usually major abdominal open surgery; its success depends on multiple factors, including the woman's current age and the age at which she had the tubal ligation and the skill of the surgeon.

See also CONCEPTION; FAMILY PLANNING; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; VASECTOMY.

Turner's syndrome A spontaneous (nonhereditary) chromosomal disorder in which there are abnormalities of the X CHROMOSOME, the SEX CHROMOSOME that establishes female gender, resulting in various anatomic and physiologic anomalies. These abnormalities may include only a single X chromosome (X chromosome deletion) instead of the normal pair of X chromosomes, or one complete and one fragmented or partial X chromosome. As well, the pattern may be mosaic, with

some cells in the body carrying the normal paired X chromosome complement and others carrying the abnormality. Turner's syndrome affects only females.

Though symptoms of Turner's syndrome vary depending on the severity of the chromosomal abnormality, characteristic traits include very short stature and loss or lack of ovarian function. An unusually short neck with webbed SKIN, and a broad, shield-shaped chest may be prominent at birth to suggest the presence of Turner's syndrome though often the diagnosis comes later in childhood or early ADOLESCENCE when SECONDARY SEXUAL CHARACTERISTICS fail to develop. GENETIC TESTING (KARYOTYPE) confirms the diagnosis. Anomalies of the HEART (coarctation of the AORTA) and KIDNEYS (HORSESHOE KIDNEY) are also common. As adults, women who have Turner's syndrome have increased risk for type 2 DIABETES, HYPOTHYROIDISM (underactive THYROID GLAND function), HYPERTENSION (high BLOOD PRESSURE), and OSTEOPOROSIS.

HORMONE THERAPY with ESTROGENS and progestin from PUBERTY through midlife (to the age MENOPAUSE would normally occur, around 50) is the standard course of treatment for Turner's syndrome. This treatment causes relatively normal development of secondary sexual characteristics and sometimes of ovarian function to produce hormones, though the OVARIES do not produce normal OVA. In mosaic Turner's syndrome, the woman's ovaries may function until early adulthood. ASSISTED REPRODUCTIVE TECHNOLOGY (ART) techniques can make PREGNANCY possible. There are no measures to prevent Turner's syndrome.

See also CHROMOSOMAL DISORDERS; GENETIC DISORDERS; KLINEFELTER'S SYNDROME; MOSAICISM.



umbilical cord The entwinement of the two umbilical arteries, one umbilical VEIN, and nerves that extend from the PLACENTA to the developing FETUS during PREGNANCY. The length of the umbilical cord varies according to numerous factors. The flow of BLOOD through the umbilical arteries and vein holds the umbilical cord relatively rigid. A thick gelatinous coating, called Wharton's jelly, surrounds the umbilical cord to protect it as it floats in the AMNIOTIC FLUID.

The umbilical cord carries nourishment from the mother to the fetus and metabolic waste from the fetus to the mother via the blood circulation. The umbilical cord enters the fetus in the center of its abdomen. The umbilical arteries carry blood from the fetus to the placenta, which delivers oxygen and NUTRIENTS to the blood. The umbilical vein then carries the oxygenated blood back to the fetus.

The third stage of childbirth is delivery of the placenta, often called the afterbirth. When the woman delivers the umbilical cord the doctor or midwife clamps it in two places, cuts between the clamps, and seals the end attached to the baby with a plastic clip. Within two to three weeks the stump of the umbilical cord shrivels, hardens, and falls off. In its place remains the SCAR that forms to close off the umbilical portal into the infant's body, the umbilicus or navel (commonly called the belly button). The remnants of the umbilical arteries and umbilical vein become ligaments within the abdomen.

For further discussion of the umbilical cord within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also ARTERY; BLOOD STEM CELLS; NERVE.

uterine fibroids Benign (noncancerous) tumors of connective tissue and MUSCLE that grow from the walls of the UTERUS. Uterine fibroids, also called uterine leiomyomas or fibromyomas, may grow inward into the inner cavity of the uterus (submucosal fibroids), within the layers of the myometrium (muscular wall of the uterus), or outward from the myometrium into the abdominal cavity (subserosal fibroids). Pedunculated fibroids grow on stalks and can be submucosal or subserosal.

Uterine fibroids are very common. They may occur as isolated or clustered growths ranging in size from barely visible to the eye to as big as grapefruit. Uterine fibroids may cause symptoms when they press against other abdominal structures such as the BLADDER OR RECTUM, when a pedunculated fibroid twists on its stalk, or when a fibroid dies and releases fluid and debris that irritates the surrounding tissues.

Symptoms and Diagnostic Path

Three fourths of women who have uterine fibroids have no symptoms; the doctor detects the fibroids during routine PELVIC EXAMINATION OR ULTRASOUND performed for other reasons. When symptoms occur they often include

- low abdominal (pelvic) pressure OR PAIN that often intensifies during MENSTRUATION
- heavy or prolonged menstrual bleeding
- bleeding between menstrual periods
- CONSTIPATION OR DIARRHEA
- pain in the lower back or the upper legs

Uterine fibroids may also create FERTILITY problems when they are large enough or when they

grow in positions, especially near the openings of the FALLOPIAN TUBES, that prevent the implantation of a fertilized egg (ZYGOTE). Large fibroids may interfere with the growth of the FETUS, causing spontaneous ABORTION (miscarriage).

The diagnostic path includes pelvic examination and imaging procedures such as ultrasound, COMPUTED TOMOGRAPHY (CT) SCAN, OR MAGNETIC RESONANCE IMAGING (MRI). The doctor may also perform HYSTEROSCOPY to view the inner uterus or laparoscopy to view the abdominal cavity. These procedures, performed with ANESTHESIA, also allow the doctor to also take small samples of the growths for further laboratory analysis.

Treatment Options and Outlook

Uterine fibroids that do not cause symptoms do not require treatment. Often, uterine fibroids shrink on their own with MENOPAUSE and then cease to cause symptoms. Medical treatments include

- NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), which effectively relieve the discomfort of uterine fibroids when symptoms are mild
- hormones such as GONADOTROPIN-RELEASING HORMONE (GNRH) agonists (such as leuprolide) and ANDROGENS (such as Danocrine) that alter the hormonal balance in the body, causing the fibroids to shrink
- oral contraceptives (birth control pills), particularly progestin-only products, which may reduce symptoms with fewer risks and side effects than other HORMONE therapies

These drugs all have significant side effects and affect fertility during the course of treatment. Though these medications are effective, a woman can take them for only a limited time and the fibroids rapidly return when she stops taking the medication.

Surgical treatment options include removal of the fibroids (myomectomy), which preserves fertility, and removal of the uterus (HYSTERECTOMY), which ends fertility. Uterine fibroid embolization (UFE) is an option for some fibroids. For this procedure an interventional radiologist injects sterile polyvinyl alcohol (PVA) particles through a catheter inserted into the femoral ARTERY in the

groin and threaded into the arteries that supply the fibroids. The particles block the arteries, cutting off the fibroid's BLOOD supply and causing it to die.

Risk Factors and Preventive Measures

Uterine fibroids are most common in women who are between ages 30 and 40. Though the cells that form uterine fibroids have more estrogen receptors (molecules that accept, or bind with, ESTROGENS) than normal myometrial cells and most fibroids recede with menopause, the correlation between estrogen and fibroids remains unclear. There are no measures to prevent uterine fibroids from developing.

See also [ADENOMYOSIS](#); [ENDOMETRIOSIS](#); SURGERY BENEFIT AND RISK ASSESSMENT.

uterine prolapse A circumstance in which the ligaments and muscles that support the UTERUS within the abdomen weaken, allowing the uterus to sag into the VAGINA. The weakness generally occurs as a consequence of multiple pregnancies that stress them or traumatic CHILDBIRTH that causes damage to them. OBESITY increases the risk for uterine prolapse. Less commonly, uterine prolapse may develop in a woman who has long-term chronic COUGH such as may occur with chronic BRONCHITIS OR CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD).

The symptoms of uterine prolapse may include

- sensation of heaviness or pressure in the lower pelvis
- PAIN during SEXUAL INTERCOURSE
- lower BACK PAIN

Depending on the severity of the prolapse, the uterus and cervix may protrude into the vagina or through the entrance of the vagina (vaginal introitus). The diagnostic path includes PELVIC EXAMINATION, which is typically sufficient for the doctor to diagnose uterine prolapse.

Treatment for mild to moderate uterine prolapse is most often a vaginal pessary, a fitted device the woman inserts into her vagina to hold the uterus in position. Treatment for moderate to severe uterine prolapse is surgery either to repair the muscles and ligaments (sacral colpopexy) or to

remove the uterus (HYSTERECTOMY). Surgery provides permanent correction, though in some women the damage to the pelvic structures may later experience vaginal prolapse (sagging of the vaginal walls).

See also AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; CYSTOCELE; LIGAMENT; MUSCLE; PREGNANCY; RECTOCELE; SURGERY BENEFIT AND RISK ASSESSMENT.

uterus The hollow muscular organ that supports and contains a PREGNANCY. Eight ligaments—one anterior, one posterior, two round, two broad (also called lateral), and two uterosacral—suspend the pear-shaped uterus in the lower central abdomen (pelvis), with the narrow end of the uterus angled somewhat downward. This suspension system allows the uterus, also called the womb, to expand during pregnancy. The FALLOPIAN TUBES join the uterus, one on each side of the wide upper section called the fundus. The fundus angles forward such that the uterus lies above the urinary BLADDER.

The lower section of the uterus is the CERVIX, a thick neck of muscular tissue that joins the uterus with the VAGINA, the passage to the outside of the body. In its nonpregnant state the uterus is about three inches long and an inch thick; in PREGNANCY the uterus expands to become nearly 10 times as large as its nonpregnant size. Within four to six weeks after CHILDBIRTH the uterus returns to nearly its prepregnant size. The uterus has two layers of structure: the outer myometrium and the inner endometrium.

The surgical OPERATION to remove the uterus is HYSTERECTOMY, which may be treatment for ENDOMETRIAL CANCER, severe ENDOMETRIOSIS or UTERINE FIBROIDS, or DYSFUNCTIONAL UTERINE BLEEDING (DUB).

The myometrium The myometrium is three layers of strong, smooth (involuntary) MUSCLE. The fibers of the innermost layer form two circular

patterns that emanate from the fallopian tubes and extend to the cervix. The fibers of the middle layer occur in random patterns that run lengthwise, widthwise, and diagonally. These fibers primarily support the network of BLOOD vessels that nourish the myometrium. The outermost layer's fibers wrap diagonally (transversely) around the uterus.

The myometrium grows during pregnancy to accommodate the growing and enlarging FETUS. Through mechanisms doctors do not fully understand, the myometrium begins rhythmic and increasingly intense waves of contractions, synchronized across the three layers of muscle, that ultimately result in childbirth. The contractions stretch and thin (efface) the cervix and then push the fetus through the cervix, into the vagina, and out of the body.

The endometrium The inner structure of the uterus is the endometrium, a membranous tissue that contains abundant blood vessels and glands. The endometrium responds to the monthly hormonal cycle of estrogen and PROGESTERONE peaks and troughs, thickening when blood levels of ESTROGENS rise—a preparation for pregnancy—and sloughing when estrogen drops and progesterone rises—MENSTRUATION. When these hormonal cycles cease with MENOPAUSE, the endometrium enters a state of atrophy, in which it remains for the rest of the woman's life.

HEALTH CONDITIONS THAT CAN AFFECT THE UTERUS

ADENOMYOSIS	DYSFUNCTIONAL UTERINE BLEEDING (DUB)
ENDOMETRIAL CANCER	ENDOMETRIAL HYPERPLASIA
ENDOMETRIOSIS	PELVIC INFLAMMATORY DISEASE (PID)
PREGNANCY	UTERINE FIBROIDS

For further discussion of the uterus within the context of the structures and functions of reproduction and sexuality, please see the overview section “The Reproductive System.”

See also HYSTEROSCOPY; OVARIES; SEXUAL HEALTH.

V-Z

VACTERL The acronym for a constellation of BIRTH DEFECTS that tend to occur in coincidence with each other. Doctors consider a baby who has three or more of the defects to have the VACTERL association, and will examine the baby closely for the other defects in the constellation. These defects include

- V: vertebral (spinal) anomalies
- A: ANAL ATRESIA (also called imperforate ANUS)
- C: cardiac (HEART) anomalies
- T/E: tracheoesophageal fistula (may also occur as tracheal fistula and ESOPHAGEAL ATRESIA)
- R: renal (kidney) anomalies
- L: limb anomalies

Occurring often enough that some doctors believe it, too, is part of the constellation, is a single-ARTERY UMBILICAL CORD (the normal umbilical cord has two arteries), which sometimes appears in the acronym as a final S (VACTERLS). VACTERL occurs sporadically (in a nonhereditary pattern); researchers do not know what causes it, nor do they understand the connections among the various defects. Some of the birth defects can be life threatening, such as the HEART malformation tetralogy of Fallot (a complex of four serious heart defects). Treatment, often surgery, attempts to correct the congenital anomalies.

See also CONGENITAL ANOMALY; CONGENITAL HEART DISEASE.

vagina The muscular passageway between the CERVIX and the VULVA (outside of the body). The vagina serves as the portal through which the menstrual flow leaves the body with MENSTRUATION, the erect PENIS enters during SEXUAL

INTERCOURSE, and the FETUS passes during CHILDBIRTH.

The outer structures of the vagina are strong muscles that have the ability to vary the inner diameter of the vagina from its normal state in which the vaginal walls touch each other to four or five inches to accommodate the birth of a child. Deep folds of mucous membrane (the vaginal mucosa) line the vagina. The folds, called rugae, give the vagina its ability to expand. The vaginal muscles also relax to extend the depth (length) of the vagina, facilitating SEXUAL INTERCOURSE.

The vaginal tissue near the opening of the vagina (the vaginal introitus) has an abundance of sensory NERVE endings though the rest of the vaginal mucosa has few sensory nerve endings. A small ring of vaginal mucosa, called the hymen, extends partially across the opening of the vagina. The degree to which the hymen restricts access to the vagina varies widely among women. Though conventional wisdom purports that penetration of the erect penis with a woman's first experience of sexual intercourse tears or ruptures the hymen, this may or may not be the case. A hymen that does not extend very far across the vaginal opening may not impede the entry of the erect penis. The hymen may also rupture or tear as a result of other factors such as insertion of tampons or activities such as horseback riding.

The Bartholin's glands and Skene's ducts near the entrance to the vagina and the nabothian glands (cervical glands) that cover the cervix provide secretions to moisten and lubricate the interior of the vagina. These secretions diminish with the loss of ESTROGENS that characterizes MENOPAUSE. As a result the vaginal mucosa becomes thin and fragile and the vagina less flexible after menopause.

HEALTH CONDITIONS THAT CAN AFFECT THE VAGINA

CANDIDIASIS (vaginal yeast infection)	CHLAMYDIA
<i>Escherichia coli</i> infection	GENITAL HERPES
GENITAL TRAUMA	GONORRHEA
HUMAN PAPILLOMAVIRUS (HPV)	SEXUAL ASSAULT
vaginal cancer	VAGINITIS

For further discussion of the vagina within the context of the structures and functions of reproduction and sexuality, please see the overview section “The Reproductive System.”

See also AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; BARTHOLIN’S CYST; COLPOSCOPY; MENSTRUAL CYCLE; NABOTHIAN CYST; SEXUAL HEALTH; SEXUALLY TRANSMITTED DISEASES (STDs).

vaginitis INFLAMMATION of the VAGINA that may occur as a result of irritation or INFECTION. Common causes of irritation-based vaginitis include douches, feminine hygiene products, spermicides, bubble bath, and soaps. Common causes of infection-based vaginitis include CANDIDIASIS (yeast infection) and SEXUALLY TRANSMITTED DISEASES (STDs) such as CHLAMYDIA and TRICHOMONIASIS. Viruses that may cause vaginitis include HERPES SIMPLEX 2 (HSV-2), which causes GENITAL HERPES, and HUMAN PAPILLOMAVIRUS (HPV), which may cause clusters of wartlike growths. Other forms of vaginitis are bacterial (called gardnerella) and atrophic (which may occur after menopause).

Symptoms and Diagnostic Path

The symptoms of vaginitis typically include itching, burning, soreness, or other discomfort. When the cause is infection there may be a discharge or unusual odor. The diagnostic path includes discussion of sexual activity and any history of STDs, PELVIC EXAMINATION with PAP TEST, and laboratory examination or culture of any discharge to check for infection.

Treatment Options and Outlook

Treatment depends on the identified cause of the vaginitis and may include ANTIBIOTIC MEDICATIONS for bacterial infection (including STDs) or ANTIFUNGAL MEDICATIONS for yeast infection. When the cause is irritation, removing exposure to the source (such as a douche solution or spermicide) allows the vaginal tissues to heal. The doctor may

prescribe topical CORTICOSTEROID MEDICATIONS to relieve symptoms. Tepid baths in water containing baking soda are often soothing. Wearing loose-fitting cotton underwear and avoiding pantyhose are other helpful measures. Most vaginitis improves rapidly with appropriate treatment.

Risk Factors and Preventive Measures

Vaginitis is very common in women, particularly women who are sexually active. SEXUAL INTERCOURSE, particularly with multiple sex partners or unprotected (without a barrier such as a condom), increases the risk for vaginitis. Women who use intrauterine devices (IUDs) for CONTRACEPTION also have increased risk for vaginitis as well as PELVIC INFLAMMATORY DISEASE (PID). Vaginitis is uncommon in prepubertal girls (girls who have not yet begun to menstruate) though may result from *ESCHERICHIA COLI* INFECTION as a consequence of poor toileting hygiene. Preventive measures include minimizing exposure to potential irritants and wearing clothing that allows some airflow between the fabric and the external GENITALIA.

See also PERSONAL HYGIENE; SEXUAL HEALTH; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION.

varicocele A VARICOSE VEIN in the testicle. Varicose veins are dilated, twisted, and often nonfunctioning veins that develop for numerous reasons. Varicocele affects the BLOOD flow that leaves the TESTICLES. Blood that accumulates in the testicles can raise the temperature within the SCROTUM high enough to interfere with proper SPERM formation (spermatogenesis) and maturation, resulting in INFERTILITY. A man may notice a varicocele as a soft bulge in his testicle that becomes more prominent when bearing down. Varicocele is more common in the left testicle because of the structure of the veins. The doctor can detect varicocele on palpating the testicles; Doppler ULTRASOUND, which shows the flow of blood, confirms the diagnosis.

Treatment is surgery to repair the varicocele. The OPERATION is an AMBULATORY SURGERY (the man goes home the same day). The man may receive general or regional ANESTHESIA. The most common operative technique involves a small incision made into the lower portion of the groin through which the surgeon can reach and repair the varicocele. HEALING is rapid and most men return to

regular activities, including sexual activity, within two weeks. When varicocele is the cause of infertility, FERTILITY usually returns when the surgical wound heals.

See also SPERMATOCELE; SURGERY BENEFIT AND RISK ASSESSMENT.

vas deferens A narrow tube that carries SPERM from the epididymis to the ejaculatory duct during ORGASM and EJACULATION. One vas deferens, also called a ductus deferens, arises from each testicle. The smooth-MUSCLE walls of the vas deferens contract and relax in wavelike movements to propel sperm from the testicle to mix with seminal fluid, which then carries the fluid (SEMEN) from the PENIS during ejaculation.

For further discussion of the vas deferens within the context of the structures and functions of reproduction and sexuality, please see the overview section “The Reproductive System.”

See also FERTILITY; TESTICLES; VASECTOMY.

vasectomy A surgical OPERATION to sever (cut) the VAS DEFERENS, the narrow tubes that carry SPERM from a man’s TESTICLES to the ejaculatory ducts where the sperm mixes with seminal fluid in preparation for EJACULATION (ejection from the PENIS during ORGASM). One vas deferens extends from each testicle, running very close beneath the surface of the SKIN of the SCROTUM.

Surgical Procedure

There are two methods for performing vasectomy, both of which are outpatient procedures usually done in the doctor’s office. Each begins with the doctor injecting local ANESTHESIA into the scrotum to numb the area. For conventional vasectomy the doctor then makes two small incisions, one on each side of the scrotum, or a single incision at the base of the scrotum. Each vas deferens is accessible through the incision. The doctor cuts each vas deferens, removes a small segment to separate the ends, and sutures (stitches) the ends closed. The doctor then places several small, dissolving sutures to close the incisions in the scrotum.

For the nonsurgical or no scalpel vasectomy, the doctor locates and clamps the vas deferens through the skin of the scrotum using a special

instrument called a ringed extracutaneous vas clamp. The clamp closes in a small circle; each tip is sharp. When closed the clamp makes a tiny puncture in the scrotum and pulls the vas deferens through the surface. The doctor cuts the exposed vas deferens, ties or cauterizes the ends, and tucks the sealed ends back inside the scrotum. The puncture heals without sutures. The doctor repeats the procedure on the other side.

Risks and Complications

Some swelling and discomfort is normal during the first 24 to 48 hours after the vasectomy. Ice to the scrotum and one of the NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) such as ibuprofen help relieve INFLAMMATION and PAIN. Wearing tight-fitting briefs or an athletic supporter for a few days gives additional support to the scrotum to minimize discomfort. Excessive bleeding and INFECTION are uncommon though can occur, as with any surgical operation. Some men experience HEMATOMA (collection of BLOOD within the scrotum) and GRANULOMA (SCAR tissue formation) after vasectomy. Most hematomas reabsorb within a week. Granulomas develop in reaction to sperm that leak into the tissues within the scrotum from the cut end of the vas deferens. Though granulomas are not harmful, they may remain tender or even painful for several weeks to several months.

Sperm may remain in the seminal ducts and other structures for quite some time, so a vasectomy is not effective immediately. A man must have two negative sperm counts one to two months after the vasectomy (or after 10 to 20 ejaculations) before he can consider himself infertile. It is essential to use an alternative method of CONTRACEPTION during this time. Because reanastomosis (also called recanalization) may occur years to decades after vasectomy, a man who has had a vasectomy should have periodic sperm counts throughout life to confirm that he remains infertile.

Outlook and Lifestyle Modifications

Vasectomy renders a man permanently infertile (sterile) by blocking the route by which sperm travel out of the testicles. Spermatogenesis (production of new sperm cells) continues; the body

eventually reabsorbs the sperm. Vasectomy does not alter a man's sexual desire or erectile function (ability to have an **ERECTION**). The ejaculate contains about the same amount of **SEMEN** as before vasectomy; the semen does not contain sperm, which slightly reduces its volume. There is a very slight risk for spontaneous reanastomosis (reconnection of the cut ends of the vas deferens) that can result in unexpected **FERTILITY**. Surgery to reverse vasectomy is sometimes possible to restore fertility, though multiple variables affect its success. Men should consider the loss of fertility with vasectomy to be permanent. Vasectomy does not provide protection against infection with **SEXUALLY TRANSMITTED DISEASES (STDs)** or **HIV/AIDS**.

See also **FAMILY PLANNING**; **SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION**; **SURGERY BENEFIT AND RISK ASSESSMENT**; **TUBAL LIGATION**.

VBAC Vaginal birth after **CESAREAN SECTION**. In cesarean section, the obstetrician makes a surgical incision through the wall of the **UTERUS** to deliver the baby, then sutures (stitches) the incision closed. The **SCAR** that forms when the surgical wound heals is somewhat weaker than the surrounding **MUSCLE** of the uterus. When the incision is low and horizontal (transverse) in the uterus this slight weakness has little consequence. If the uterine incision runs vertically, however, there is an increased risk that the wall of the uterus could rupture along the scar during the intense contractions of labor and delivery. Uterine rupture is life threatening for the woman and the baby.

The obstetrician attempts to assess the likelihood of uterine rupture as the woman's **PREGNANCY** becomes advanced. The risk for uterine rupture is high enough with a vertical uterine scar that most obstetricians strongly discourage the woman from attempting vaginal delivery with subsequent pregnancies. If the obstetrician believes the risk for uterine rupture is low, which is usually the case with the low horizontal scar, **VBAC** is of little additional risk for the woman. Other factors that may influence the decision between a woman and her obstetrician about **VBAC** include the reason for the previous cesarean section and the woman's overall health status in her current pregnancy. About half of women who have cesarean deliver-

ies are able to have vaginal deliveries in subsequent pregnancies.

See also **CHILDBIRTH**; **PRENATAL CARE**.

vulva See **GENITALIA**.

vulvodynia Chronic and sometimes severe **vulvar PAIN** a woman experiences. Though many women who have vulvodynia have had chronic or recurrent **VAGINITIS** (vaginal infection), the connection between vaginitis and vulvodynia is unclear and only a small percentage of women who have vaginitis develop vulvodynia. There are few other discernible circumstances that could account for the symptoms of vulvodynia; doctors most often consider vulvodynia a **CHRONIC PAIN syndrome**.

The symptoms of vulvodynia often come on suddenly and may include

- intense burning, stinging, or itching of the vulva (labia, **CLITORIS**, and opening to the **VAGINA**)
- discomfort and soreness when sitting or walking
- **PAIN** during **SEXUAL INTERCOURSE** (dyspareunia)

The diagnostic path includes a thorough **PELVIC EXAMINATION** with cultures for yeast infection (**CANDIDIASIS**) and **SEXUALLY TRANSMITTED DISEASES (STDs)** such as **GONORRHEA** and **CHLAMYDIA**. In vulvodynia, such test results are negative and the pelvic examination is normal. Treatment options include medications such as **ANTIHISTAMINE MEDICATIONS**, which lessen itching, and **tricyclic ANTIDEPRESSANT MEDICATIONS**, which act to block **NERVE** impulses related to pain. Other medications sometimes helpful for the pain of vulvodynia include certain antiseizure medications and topical **CORTICOSTEROID MEDICATIONS**. Other methods of pain relief that some women find helpful include cold compresses to the vulva, **BIOFEEDBACK**, **ACUPUNCTURE**.

Vulvodynia may persist for several months; rarely, symptoms may continue for more than a year. Eliminating any underlying causes for symptoms generally speeds recovery from vulvodynia as well. Relaxation techniques and compassionate communication between the woman and her sexual partner help with the emotional and sexual aspects of vulvodynia.

See also [ALTERNATIVE METHODS FOR PAIN RELIEF](#); [ANALGESIC MEDICATIONS](#); [MALDYNIA](#); [SEXUALLY TRANSMITTED DISEASE \(STD\) PREVENTION](#).

zygote The cell that results when a spermatozoon (SPERM cell) penetrates an ovum (egg cell) during fertilization. Each GAMETE (sperm and ovum) is a haploid cell; it contains one half the genetic material necessary to support life. The zygote is a diploid cell; it contains all the DNA necessary to create a new life. Fertilization typically takes place in the fallopian tube. The zygote grows and divides as it makes its way through the fallo-

pian tube to the UTERUS, a journey of about five days. When it reaches the uterus the zygote implants into the endometrium, the thick, BLOOD-rich lining of the uterus. By the time implantation is complete the zygote has become a two-layered structure called a blastocyst.

For further discussion of the zygote within the context of the structures and functions of reproduction and sexuality, please see the overview section “The Reproductive System.”

See also [ASSISTED REPRODUCTIVE TECHNOLOGY \(ART\)](#); [CELL STRUCTURE AND FUNCTION](#); [EMBRYO](#); [FALLOPIAN TUBE](#); [FETUS](#); [OVA](#).

PSYCHIATRIC DISORDERS AND PSYCHOLOGIC CONDITIONS

Psychiatry and psychology are disciplines within the practice of health care that deal with mental illness. Health-care professionals who provide care for people who have mental illnesses include psychiatrists, who are physicians (MDs or DOs); psychologists (PhDs); master's level therapists such as counselors (sometimes also called psychologists); social workers; and clinical registered nurse practitioners (CNRPs) who specialize in mental health. In the United States licensing requirements and practice limitations for mental health practitioners vary among states, though in all states only psychiatrists may prescribe medications.

This section, "Psychiatric Disorders and Psychologic Conditions," presents an overview discussion of mental health and mental illness and includes entries about psychiatric disorders, psychologic conditions, and their treatments. The section "The Nervous System" contains overview discussion and comprehensive entries about conditions that affect cognition, memory, and thought processes that arise from disease or injury to BRAIN structures that alters brain function.

Finding the Line between Mental Health and Mental Illness

Psychiatric disorders and psychologic conditions are those that doctors generally define as illnesses that arise from disrupted thought processes and their corresponding behaviors. However, the causes of mental illness remain poorly understood. Most psychiatric disorders reflect a mix of biochemical, behavioral, and genetic components. About 80 percent of people who have BIPOLAR DISORDER, for example, have other family members who have either bipolar disorder or clinical DEPRESSION that requires treatment.

The diagnosis of mental illness is often a significant challenge. One issue is that many of the symptoms that characterize mental illness are thoughts, feelings, and behaviors that everyone experiences to certain degree. However, in many situations it is less the symptoms themselves and more the level of dysfunction the symptoms cause

in the person's life that defines the line between mental health and mental illness.

For example, a person may sometimes engage in speaking as though in conversation with another person when no one else is in fact present or talking, but knows the dialogue is a process of thinking aloud and can willingly start and stop the behavior. The behavior may appear amusing or quirky to others but does not interfere with the person's ability to interact with other people and to function in the world and thus in itself does not constitute mental illness.

It is a different picture when a person engages in dialogue with voices no one else can hear, but believes the voices are real and thus cannot control his or her interactions with them. In such a situation the person may believe the voices provide instruction or guidance, and behaves as though following directions the voices give. The messages from the voices may be nonsensical, confusing, demanding, or demeaning to the person and characteristically interfere with the person's ability to function in the world. This behavior represents a clear break with reality and interferes with the person's ability to function in the world and thus constitutes mental illness.

The Diagnostic Path for Psychiatric Disorders and Psychologic Conditions

The diagnostic path for mental illness begins with the elimination of potential physical or physio-

logic causes for symptoms. Loss of inhibition, for example, may occur as a consequence of STROKE, ALZHEIMER'S DISEASE, OR BRAIN TUMOR. There is a high correlation between untreated HYPOTHYROIDISM and bipolar disorder. When the doctor can eliminate physical causes, the emphasis shifts to psychologic evaluation to identify the disorder. Because many psychologic conditions and psychiatric disorders have overlapping symptoms, distinguishing among them is often a challenge.

In the United States most providers and insurance companies follow the diagnostic criteria and treatment algorithms detailed in the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders*, commonly called the DSM. The current version of the DSM includes a Roman numeral in the title to differentiate it from previous versions; for example, DSM-IV indicates the fourth version. Though other diagnostic criteria and treatment methods are available and valid, the DSM reflects the conventional perspective and is widely accepted as the standard.

Treatment and Outlook for

Psychiatric Disorders and Psychologic Conditions

The mainstays of treatment for psychiatric disorders and psychologic conditions are medications and therapy. As is the case with numerous physical health conditions, treatment often cannot cure the condition and so aims to instead manage symptoms. A person who has HYPERTENSION (high BLOOD PRESSURE) often needs lifelong antihypertensive medications and lifestyle modifications to

support cardiovascular health (such as WEIGHT LOSS AND WEIGHT MANAGEMENT and nutritious EATING HABITS). This therapeutic approach regulates the body's functions in regard to BLOOD pressure though does not end the underlying factors causing the hypertension. Likewise, a person who has bipolar disorder may need lifelong mood stabilizing medications in combination with PSYCHOTHERAPY and lifestyle measures to limit exacerbations of symptoms.

Combinations of different types of medications are common because the boundaries of many mental disorders are not clear cut and the biochemical functions that underlie them are similar. Both depression and anxiety often respond to treatment with selective serotonin reuptake inhibitor (SSRI) antidepressants, for example, even though they present different symptoms. As well, some mental disorders, such as SCHIZOPHRENIA and bipolar disorder, have multiple components that often require different types of medication to moderate symptoms.

Because most psychiatric disorders and psychologic conditions result from multiple factors, including genetic and physiologic, there is usually no way to prevent them from occurring. Many conditions respond to treatment to manage symptoms so that the condition has a negligible effect on the person's QUALITY OF LIFE. Some short-term, reactive, or narrowly defined conditions such as BRIEF REACTIVE PSYCHOSIS, POST-TRAUMATIC STRESS DISORDER (PTSD), or certain phobias are curable with appropriate treatment.

acute stress disorder A dissociative state (mental framework that creates emotional and psychologic distance from the trauma) that occurs in reaction to a traumatic event. Symptoms often begin within hours of the event and may last for a few hours to a few days. The person may speak about the trauma in the third person as though it happened to someone else, may act as though the trauma did not occur, may be unable to remember the event (dissociative amnesia), or may have an apparent lack of emotional response regarding the event. The person may appear dazed and “out of it” or have acute and severe symptoms of DEPRESSION or anxiety. Flashbacks and dreams in which he or she relives the traumatic event are common. Normal, everyday circumstances may also trigger flashbacks.

Diagnosis is usually straightforward because the connection between the traumatic event and the symptoms is clear. Treatment may include supportive therapy along with short-term ANTIANXIETY MEDICATIONS or ANTIDEPRESSANT MEDICATIONS. Rarely, the symptoms continue for as long as several weeks, though psychiatrists are more likely to diagnose continuing symptoms as POST-TRAUMATIC STRESS DISORDER (PTSD).

See also BRIEF REACTIVE PSYCHOSIS; CHILD ABUSE; DOMESTIC VIOLENCE; ELDER ABUSE; GENERAL ANXIETY DISORDER (GAD); GRIEF; SEXUAL ASSAULT; STRESS AND STRESS MANAGEMENT; VIOLENCE.

antianxiety medications Medications to relieve symptoms of anxiety disorders. About 15 percent of adults in the United States have anxiety disorders for which they take antianxiety medications. There are two types of antianxiety medications in use today, the BENZODIAZEPINES and buspirone. As well, many of the ANTIDEPRESSANT MEDICATIONS,

notably the selective serotonin reuptake inhibitors (SSRIs), also successfully relieve the anxiety symptoms.

The first medications to treat anxiety were barbiturates, which produce a fairly substantial level of sedation, particularly at the onset of treatment. Barbiturates, commonly called tranquilizers, are also highly addictive and have significant risk for death due to OVERDOSE. For these reasons doctors no longer prescribe barbiturates to treat anxiety. Meprobamate was the first medication developed specifically to treat anxiety disorders. Though not chemically a barbiturate, it has many of the same actions and side effects. Doctors today occasionally prescribe meprobamate to treat anxiety in people who cannot take or do not respond to other antianxiety medications or who have coexisting psychotic disorders.

Doctors sometimes prescribe a beta blocker medication, commonly propranolol, to relieve episodic symptoms that arise specifically from performance anxiety. Beta blockers inhibit the flow of EPINEPHRINE, which prevents symptoms such as rapid HEART RATE and increased sweating. Beta blockers are not appropriate for other types of anxiety, however, because they do not affect the neurotransmitters primarily responsible for anxiety symptoms.

Benzodiazepines The first generation of benzodiazepines, chlordiazepoxide (Librium) and diazepam (Valium), came into use in the early 1960s and quickly replaced both barbiturates and meprobamate in the treatment of anxiety disorders. The benzodiazepines produce rapid relief from symptoms, some of them within hours of the first DOSE. This characteristic makes benzodiazepines useful for immediate or episodic relief of anxiety symptoms. There are now nearly a dozen

benzodiazepine drugs on the market; they differ primarily in the extent of sedation they cause, the onset of action, and the length of time they are active in the body.

BENZODIAZEPINE ANTIANXIETY MEDICATIONS

alprazolam	chlordiazepoxide
clonazepam	clorazepate
diazepam	flurazepam
halazepam	lorazepam
oxazepam	prazepam
temazepam	

Buspirone is a unique DRUG that does not belong to existing chemical classification and is primarily effective as treatment for moderate to moderately severe GENERALIZED ANXIETY DISORDER (GAD). Buspirone does not appear to be particularly effective for treating PANIC DISORDER, OBSESSIVE–COMPULSIVE DISORDER (OCD), or PHOBIA. The person must take buspirone regularly for two to three weeks before experiencing relief from anxiety symptoms.

How These Medications Work

The benzodiazepines work by binding with neuroreceptors on BRAIN neurons for gamma-aminobutyric acid (GABA), a NEUROTRANSMITTER that inhibits electrical activity. This binding extends GABA’s availability, intensifying its inhibiting actions and consequently inducing emotional and neurologic calmness and, at high enough doses, sedation. The mechanisms of buspirone are unknown, though it does not act on GABA or produce sedation at any dose.

Therapeutic Applications

Doctors commonly prescribe antianxiety medications to treat mental disorders such as GAD, ACUTE STRESS DISORDER, panic disorder, POST-TRAUMATIC STRESS DISORDER (PTSD), phobias, and OCD. Doctors may also prescribe antianxiety medications, sometimes called anxiolytics, to relieve short-term anxiety related to ALCOHOL DETOXIFICATION as well as to provide a sense of calm before minor dental and medical procedures. Many of the benzodiazepines have other clinical applications, such as MUSCLE relaxants and hypnotics (drugs that provide conscious sedation). Doctors sometimes pre-

scribe benzodiazepines to treat clonic-tonic seizures in SEIZURE DISORDERS and spasticity in disorders such as CEREBRAL PALSY and SPINAL CORD INJURY.

Risks and Side Effects

Key risks with long-term benzodiazepines are dependence and tolerance. The longer a person takes a benzodiazepine medication the more accustomed the brain becomes to it. Achieving consistent effects over time often means gradually increasing the dosage. Suddenly stopping a benzodiazepine medication after taking it for longer than six weeks may result in a withdrawal syndrome with various discomforts, including agitation, irritability, HEADACHE, and sleep disturbances. Doctors recommend tapering the dose over two or three weeks rather than abruptly stopping a benzodiazepine. Buspirone does not cause dependency or tolerance, though it also can cause unpleasant symptoms when stopped suddenly.

See also [DEPRESSION](#); MUSCLE RELAXANT MEDICATIONS; VALERIAN.

antidepressant medications Medications primarily to treat depression. About 25 percent of adults in the United States have depression and more than 80 percent of them take antidepressant medications. There are several classifications, also called generations, of antidepressant medications. The drugs in each classification work by somewhat different mechanisms from those in other classifications.

Researchers have linked antidepressant use in children and teenagers with increased risk for suicide. The US Food and Drug Administration (FDA) requires warnings on the labels of drugs for which this risk is significant and cautions parents to closely observe children who take antidepressant medications for signs of increased DEPRESSION or expressions of interest in suicide.

Monoamine oxidase inhibitors (MAOIs)

Researchers developed the first antidepressant medications, the MAOIs, in the early 1950s. This class of antidepressant works by a somewhat dif-

ferent mechanism from subsequent classes in that it blocks the function of an enzyme (monoamine oxidase, or MAO) to indirectly extend the availability of the neurotransmitters DOPAMINE, NOREPINEPHRINE, and serotonin. Unfortunately, the body requires MAO to metabolize tyramines, proteins that occur naturally in certain foods. Unmetabolized tyramines affect cardiovascular function and can cause rapid, extreme elevations in BLOOD PRESSURE, which presents a significant risk for STROKE. People taking MAOIs must avoid eating foods high in tyramines, such as smoked meats, cheeses, wines, and fermented or pickled foods. Because the risk for potentially fatal HYPERTENSION (high blood pressure) is so high, doctors prescribe MAOIs primarily as a final treatment option when other antidepressant medications do not improve symptoms.

MONOAMINE OXIDASE INHIBITOR (MAOI) ANTIDEPRESSANTS	
isocarboxazid	phenelzine
tranylcypromine	

Tricyclics The tricyclic class of antidepressants, so-called because of their three-ringed molecular structure, entered the market in the early 1960s as a welcome alternative to MAOIs. This second generation of antidepressants became the most widely prescribed antidepressant medications for 30 years, leading treatment protocols until selective serotonin reuptake inhibitors (SSRIs) supplanted them in the 1980s. Tricyclics, also called TCAs, appear to selectively suppress serotonin and norepinephrine reuptake, though the precise mechanisms by which they do so remain unknown.

Doctors may prescribe tricyclic antidepressants to treat other health conditions, notably ENURESIS (bedwetting), OBSESSIVE–COMPULSIVE DISORDER (OCD), CHRONIC FATIGUE SYNDROME, and some CHRONIC PAIN syndromes such as FIBROMYALGIA and chronic regional PAIN syndrome. Though an improvement over MAOIs, with their multitude of side effects, the tricyclic antidepressants have some significant side effects of their own, most bothersome among them being drowsiness, dry MOUTH, CONSTIPATION, and SEXUAL DYSFUNCTION. Doctors now tend to prescribe tricyclics as second-line treatment for depression that does not improve with SSRIs.

TRICYCLIC ANTIDEPRESSANTS	
amitriptyline	clomipramine
desipramine	doxepin
imipramine	nortriptyline
protriptyline	trimipramine

Selective serotonin reuptake inhibitors (SSRIs) The SSRIs block reuptake of only serotonin, eliminating or diminishing many of the side effects attributable to inhibited reuptake of norepinephrine, which is a feature of MAOIs and tricyclics. Doctors now prescribe SSRIs as the first line of medication treatment to treat moderate depression in most people. SSRIs are also effective in treating the EATING DISORDERS anorexia nervosa and bulimia. At lower doses than doctors typically prescribe to treat depression, SSRIs have moved to the front line of therapeutic options for treating discomforts related to MENOPAUSE such as HOT FLASHES, replacing hormone replacement therapy (HRT).

SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIs)	
citalopram	duloxetine
escitalopram	fluoxetine
fluvoxamine	paroxetine
sertraline	

Tetracyclics The tetracyclic class of antidepressants (a four-ringed molecular structure) debuted in the late 1990s as an alternative to the tricyclics. Like tricyclics, the tetracyclics extend the presence of serotonin and norepinephrine by delaying their reuptake. However, tetracyclics have fewer as well as milder side effects than tricyclics.

TETRACYCLIC ANTIDEPRESSANTS	
amoxapine	maprotiline
mirtazapine	

Other antidepressants Several new antidepressants came into use in the late 1990s and early 2000s that do not fit within conventional classifications. These drugs selectively affect specific neurotransmitters or neuroreceptors through different mechanisms from those of other antidepressants. Bupropion has US Food and Drug Administration (FDA) approval for use in SMOKING CESSATION efforts.

OTHER ANTIDEPRESSANTS

bupropion	nefazodone
trazodone	venlafaxine

How These Medications Work

Most antidepressant medications, regardless of class, work through selective reuptake inhibition: they block the natural breakdown and reassimilation of specific neurotransmitters, biochemicals that carry NERVE impulses between neurons. The result is an extended presence of the neurotransmitters, increasing the number of nerve impulses they can transport. Researchers do not know the precise mechanisms of this process, though the result is an elevation of function in the affected parts of the brain, which in the case of depression are areas concerned with mood and emotion. Though antidepressants affect neurotransmission from the first dose, noticeable changes generally do not occur until after several weeks of use.

Therapeutic Applications

The primary use of antidepressant medications is to treat moderate to severe DEPRESSION. Doctors may also prescribe antidepressants to treat BIPOLAR DISORDER, BODY DYSMORPHIC DISORDER, eating disorders, ACUTE STRESS DISORDER, POST-TRAUMATIC STRESS DISORDER (PTSD), POSTPARTUM DEPRESSION; ADDICTION recovery, SEASONAL AFFECTIVE DISORDER (SAD), and in combination with other medications to treat psychotic disorders such as SCHIZOPHRENIA. Some antidepressant medications have uses outside the realm of psychiatric disorders and psychologic conditions, such as smoking cessation, chronic pain management, and relief of menopause discomforts. Some of these are OFF-LABEL USE.

Risks and Side Effects

Though antidepressants make it possible for nearly 10 million Americans to participate fully in, and enjoy, the activities of every day life, they have substantial risks. Any antidepressant that inhibits reuptake of norepinephrine also has an effect on smooth MUSCLE function throughout the body, notably the gastrointestinal tract, genitourinary tract, and cardiovascular system. Side effects such as dry mouth, constipation, urinary hesitancy or urinary frequency, and ERECTILE DYSFUNCTION are common, though they often improve after taking

the antidepressant for three months. Though each classification of antidepressant drugs has risks and side effects that are common to all drugs in the classification, each medication also has unique risks and side effects. Often, side effects improve over time and are temporary (go away when the person stops taking the antidepressant).

Excessive serotonin levels can cause serious and potentially life-threatening symptoms, called serotonin syndrome, that affect the functions of the LIVER, HEART, KIDNEYS, and skeletal muscles. It is important not to combine SSRIs with other antidepressants or drugs, including herbal and OVER-THE-COUNTER (OTC) DRUGS, that increase serotonin levels.

Antidepressant medications interact or interfere with numerous other medications including OVER-THE-COUNTER (OTC) DRUGS, herbal, and prescription products. MAOIs interact with numerous foods, decongestant medications, ANTIHISTAMINE MEDICATIONS, and antihypertensive medications (drugs to treat high blood pressure).

See also [ANTI-ANXIETY MEDICATIONS](#); NEURORECEPTOR; PSYCHOSIS; ST. JOHN’S WORT; SUICIDAL IDEATION AND SUICIDE.

antipsychotic medications Medications to manage the symptoms of psychiatric disorders of PSYCHOSIS, including SCHIZOPHRENIA. The first of these medications, the phenothiazine DRUG chlorpromazine (Thorazine), debuted in the early 1950s and revolutionized treatment for psychotic disorders. Antipsychotic medications, also called neuroleptics, are powerful drugs that affect the ways in which the BRAIN processes information. Conventional antipsychotics are the mainstay of therapy for many psychotic disorders. Novel, or atypical, antipsychotics are newer drugs that attempt to provide a better balance between therapeutic benefit and risk of side effects. They are the first choice treatment for some moderate psychotic disorders.

How These Medications Work

Antipsychotic medications work by altering the balance of neurotransmitters (biochemicals that

conduct electrical impulses among neurons) in the brain. Most antipsychotic medications target DOPAMINE, a NEUROTRANSMITTER that is integral to the functions of thought, reasoning, memory, emotion, and mood. Though researchers do not know what causes psychotic disorders, they believe the ways in which the brain produces and uses dopamine are key factors.

ANTIPSYCHOTIC MEDICATIONS	
Conventional	
chlorpromazine	fluphenazine
haloperidol	mesoridazine
perphenazine	pimozide
prochlorperazine	thioridazine
thiothixene	trifluoperazine
trifluopromazine	
Novel (Atypical)	
aripiprazole	clozapine
loxapine	molindone
olanzapine	quetiapine
risperidone	ziprasidone

Therapeutic Applications

Doctors prescribe antipsychotic medications to treat psychotic disorders such as severe BIPOLAR DISORDER, schizophrenia, personality disorders, dissociative disorders, OBSESSIVE–COMPULSIVE DISORDER (OCD), and severe MANIA. Often a therapy regimen includes several medications that address various symptoms. Treatment with antipsychotic medications requires regular and close follow-up to monitor therapeutic effect as well as potential side effects.

Risks and Side Effects

Antipsychotic medications have numerous risks and side effects, many of which are drug specific. The most serious is neuroleptic malignant syndrome (NMS), a constellation of symptoms that may occur at any time during treatment with antipsychotic medications, although it is more likely to develop with sudden high doses. NMS follows a predictable course, starting with MUSCLE rigidity with high FEVER, confusion, and disorientation. Rapid intervention is necessary to stop the antipsychotic medications, reduce the fever, and provide appropriate medical support. Without

such intervention, there is high probability that NMS will be fatal.

Dopamine, the primary target of most antipsychotic medications, is also the primary neurotransmitter for NERVE impulses that regulate voluntary movement. Conventional antipsychotics have a broad base of effects in regard to their actions on dopamine receptors. Because of this nonspecific activity, these drugs have high risk for causing neuromuscular complications (drug-induced movement disorders). The most serious of these complications is tardive dyskinesia, a condition of involuntary, rhythmic, repetitious movements. Tardive dyskinesia is a particular risk with phenothiazines and sometimes persists even after stopping the medication. Other possible neuromuscular side effects include tremors and rigidity.

Novel, or atypical, antipsychotic medications target specific dopamine receptors found in greater numbers in the regions of the brain that regulate cognitive and emotional functions. Though novel antipsychotics can cause neuromuscular side effects with prolonged, high-dose use, the side effects are likely to be both less severe and temporary. A rare complication associated with clozapine is severe agranulocytosis, a precipitous drop in the number of white BLOOD cells called granulocytes. Granulocytes are essential for immune function. Because of the potential for this complication, people who take clozapine must have blood tests once a week for the duration of treatment plus four weeks after treatment ends to monitor their white blood cell counts.

Both conventional and novel antipsychotics interact with numerous medications, prescription as well as OVER-THE-COUNTER (OTC) DRUGS and some interact with foods. The longer a person takes antipsychotic medications, the greater the risk for complications or side effects. It is essential that the prescribing psychiatrist regularly and frequently evaluate the effectiveness of treatment and make adjustments as possible to reduce risk. For most people who have serious psychotic disorders, the QUALITY OF LIFE that medications make possible clearly outweighs their potential side effects.

See also [ANTIANXIETY MEDICATIONS](#); [ANTIDEPRESSANT MEDICATIONS](#); [DISSOCIATIVE DISORDER](#); [ELECTROCONVULSIVE THERAPY \(ECT\)](#); [GRANULOCYTE](#); [PSYCHOTHERAPY](#).

attention deficit hyperactivity disorder (ADHD)

A behavior disorder, often arising in early childhood, of marked difficulty or inability to concentrate and in particular to sit still. Though in some children symptoms are apparent early in childhood, starting school provides the first insight into ADHD for many children. Key symptoms include

- uncontrolled impulsive behavior
- difficulty listening to others
- poor attention to details
- inability to sit or stand without movement (fidgeting)
- excessive and impulsive talking

The diagnostic path includes comprehensive medical examination and **NEUROLOGIC EXAMINATION** to rule out physical causes for symptoms. Treatment is often stimulant medications such as methylphenidate, dextroamphetamine, or pemoline, which have the opposite effect of producing calm in children who have ADHD. **ANTIDEPRESSANT MEDICATIONS** are sometimes more effective for adolescents. Often parents find it beneficial to attend classes or workshops that teach methods for positive reinforcement to encourage more appropriate behaviors. ADHD may persist into adulthood, though many children outgrow most if not all of the symptoms by late **ADOLESCENCE**.

See also **CONDUCT DISORDER; OPPOSITIONAL DEFIANT DISORDER; STIMULANTS**.

autism A collective term for a spectrum of developmental disorders, also called autism spectrum disorder or pervasive developmental disorders (PDDs). Symptoms begin in early childhood, typically between the ages of 18 months and 3 years, though when parents look back on the child's infancy they can often detect earlier indications of problems. Autism ranges from mild to incapacitating in severity. Though most children experience abnormal developmental progress from birth, some appear to develop normally and then seem to suddenly disengage from social interaction. Autism is a lifelong condition that, in all but its mildest form, requires ongoing attention and treatment.

Symptoms and Diagnostic Path

The symptoms of autism become more clear as the child passes developmental markers without demonstrating the appropriate level of ability. The first pivotal marker is around age one year, by which time a child should be babbling and freely interacting with other people and his or her environment. The child who has autism, by contrast, often appears socially withdrawn and may stare at a particular toy or object for hours yet not play with it. Other characteristic indications of autism include a child who does not

- smile or make eye contact with other people
- respond to his or her name
- like to be hugged or touched
- attempt to speak or communicate with others
- understand communication efforts from others
- display attachment to or affection toward his or her parents

Many children who have autism engage in repetitious actions that are potentially harmful to themselves, such as banging their heads. The communication difficulties affect both expression and understanding; many children who have autism lack the ability to perceive emotions or to predict how others will respond. They may also fulfill their needs by simply taking what they want, which, until diagnosis, parents and other caregivers may interpret as rudeness or inconsideration. In reality it is neither; it is the only mechanism of communication available to the child at the time.

The diagnostic path includes comprehensive physical examination and **NEUROLOGIC EXAMINATION**, age-appropriate psychologic evaluations (including those specific for autism), and sometimes **GENETIC TESTING** (autism is strongly associated with **FRAGILE X SYNDROME**). Diagnosis is a process of ruling out other conditions and confirming the symptoms of developmental delay.

Treatment Options and Outlook

Treatment is most successful when it begins by age two and consists primarily of extensive therapy to provide simple, clear, and consistent structure for

the child that shapes behavior and mechanisms of communication. This approach ties in with the child's inherent need for repetition and order in his or her personal environment. Older children sometimes benefit from medications such as selective serotonin reuptake inhibitors (SSRIs), ANTIDEPRESSANT MEDICATIONS that appear to help stabilize BRAIN function in autism. Some children whose behavior is aggressive may benefit from ANTIPSYCHOTIC MEDICATIONS, and children who have significant trouble staying focused may benefit from medications used to treat ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD).

Adults who have mild autism (often called higher functioning autism or Asperger's syndrome) are often able to function in work situations, though their lack of social skills may create problems with INTERPERSONAL RELATIONSHIPS. Adults who have moderate autism generally benefit from continuation of a highly structured environment, which may mean continuing to live with parents

or other responsible adults. Adults who have severe autism often need the extensive supervision and ongoing care that living in a group home or secure, supervised residential facility provides for them.

Risk Factors and Preventive Measures

The causes of autism are unknown. There has been speculation of a correlation between thimerosal, a mercury-based preservative used in some childhood vaccines, and autism and between autism and environmental exposure to mercury as well as to lead. Researchers continue to study these potential links though so far have found no definitive evidence to clearly support or refute them. There is a known connection between the genetic disorder fragile X syndrome and autism, and researchers suspect though have yet to confirm other genetic causes.

See also GENETIC DISORDERS; HEAVY-METAL POISONING.

B

behavior modification therapy A treatment approach that focuses on changing one's actions to remedy inappropriate responses or behaviors. Behavior modification may be effective for ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD), behavior disorders, PHOBIA, SMOKING CESSATION, WEIGHT LOSS AND WEIGHT MANAGEMENT, and similar issues. The three most common types of behavior modification are

- aversion therapy, which connects the undesired action or behavior with an unpleasant experience
- positive reinforcement therapy, which connects the desired action or behavior with a pleasant experience
- desensitization, which establishes repeated, progressively extensive exposure to a circumstance that produces anxiety to diminish the anxiety response

Behavior modification therapy is most successful in treating narrowly focused conditions. Combining behavior modification therapy with

COGNITIVE THERAPY, which helps people recognize thought patterns, greatly improves its success. Therapists sometimes combine behavior modification therapy with HYPNOSIS to increase the person's receptiveness to change.

See also [PSYCHOTHERAPY](#).

bipolar disorder A pattern of alternating MANIA and DEPRESSION (manic episodes and depressive episodes) that often results in significant dysfunction and inability to participate in work and social activities. About two million Americans have bipolar disorder, sometimes called manic-depressive disorder. Though indications of bipolar disorder may be present in ADOLESCENCE, most people do not seek medical attention or receive a diagnosis until they are well into adulthood.

Symptoms and Diagnostic Path

The pattern of symptoms occurring in alternating episodes is as important as the symptoms themselves and helps distinguish bipolar disorder from either depression or mania, though many researchers believe these conditions exist along a

SYMPTOMS OF BIPOLAR DISORDER	
Symptoms of Manic Episodes	Symptoms of Depressive Episodes
euphoria and excitability	hopelessness and futility
heightened energy	diminished energy or fatigue
reduced sleep	excessive sleep
spending sprees and other behavioral indiscretions	pessimism about abilities and accomplishments
substance abuse (including ALCOHOL)	chronic physical discomforts and ailments
inability to focus or concentrate	inability to concentrate
rapid, often disjointed speech	difficulty with logic and reasoning
disorganized thoughts	loss of interest in activities, family, and friends
unrealistic perceptions of abilities and accomplishments	thoughts of suicide (suicide ideation)

continuum rather than as discreet disorders. Episodes of symptoms may last from weeks to months. Many people experience periods of normal mood between the episodes of symptoms and may experience extended time periods (sometimes years) without episodes of symptoms.

Some people experience a mix of depressive and manic symptoms with each episode, which often causes significant agitation and inability to function. Severe episodes of either depression or mania may include symptoms of psychosis (detachment from reality) such as DELUSION, HALLUCINATION, and bizarre behavior.

The diagnostic path includes comprehensive physical examination and NEUROLOGIC EXAMINATION, psychologic evaluation, and often testing for ALCOHOL or substance abuse. The doctor may also evaluate THYROID GLAND function because some people in whom manic episodes dominate have chronic HYPOTHYROIDISM (low thyroid gland function). In general, diagnostic criteria include the existence of five or more symptoms during each episode of symptoms that extend for two weeks or longer. Shorter cycles or briefer episodes may indicate similar though less severe disorders such as CYCLOTHYMIC DISORDER. Psychiatrists further classify bipolar disorder according to the pattern of symptoms:

- Bipolar I disorder is classic bipolar disorder, with depressive and manic symptoms of equal severity and length of episode.
- Bipolar II disorder features mild, short manic episodes though full depressive episodes.
- Rapid-cycling bipolar disorder features short though full-symptom cycles of episodes that occur four times a year or more frequently.

Doctors commonly consider responsiveness to treatment as affirmation of the diagnosis.

Treatment Options and Outlook

Nearly everyone who has bipolar disorder requires long-term treatment with medication to moderate symptoms. These medications include

- lithium carbonate or lithium citrate, a mood stabilizing DRUG especially effective for controlling manic symptoms

- antiseizure medications such as valproic acid (valproate), carbamazepine, gabapentin, and topiramate
- novel (atypical) ANTIPSYCHOTIC MEDICATIONS such as clozapine, olanzapine, risperidone, quetiapine, and ziprasidone, which have mood stabilizing effects
- ELECTROCONVULSIVE THERAPY (ECT) when medications are not effective or symptoms are severe
- forms of psychotherapy that help the person develop behaviors and methods for managing symptoms when they do occur
- methods to reduce stress

People who have hypothyroidism also require thyroid HORMONE supplementation; long-term treatment with lithium can cause hypothyroidism as well. Bipolar disorder is a lifelong condition that requires ongoing, consistent treatment.

Risk Factors and Preventive Measures

Family history is the most significant risk factor for bipolar disorder. However, researchers do not know what causes bipolar disorder, and there are no measures to prevent it from developing. Early diagnosis and consistent treatment are most effective for reducing the severity and disruptiveness of symptoms and often can prevent the condition from worsening.

See also STRESS AND STRESS MANAGEMENT.

body dysmorphic disorder A condition of DELUSION in which the person focuses obsessively on a slight flaw or perceived imperfection of a particular body part to the extent of persistently seeking medical care to “fix” the problem. The focus is so intense that it interferes with the person’s social and educational or professional interactions. The person may stand in front of a mirror for hours staring at the body part, engage in ritualistic behavior such as manipulating the part into the desired appearance, or refuse to go out in public without covering the part to somehow mask it. Some people avoid mirrors and reflective surfaces to the extent of refusing to go to stores or office buildings that have glass doors.

A person consumed with concern about his or her ears, for example, might spend several hours

every morning holding the ears flat against the head then letting go to see whether they've changed, repeating this behavior to the extent of missing school or work. The person may go out in public only if wearing a hat regardless of whether a hat is appropriate and may refuse to get haircuts for fear that the hair stylist will see his or her ears. The person may have multiple cosmetic surgery operations to obtain a more satisfactory appearance but is never happy with the results.

Because body image is highly subjective and most people do have minor imperfections or asymmetries in appearance, a first or even second cosmetic surgery procedure may not seem out of the ordinary. It is when the person persists in attempts to "fix" the "problem" that the dysfunction becomes apparent. The plastic surgeon or dermatologist the person consults for cosmetic surgery may be the first to raise a red flag about the person's obsession. The most successful treatment approach is medication therapy with a selective serotonin reuptake inhibitor (SSRI), a class of ANTIDEPRESSANT MEDICATIONS. Most people experience marked improvement within three months and have long-term improvement after six months to a year of medication. Combining SSRI therapy with COGNITIVE THERAPY has more rapid effectiveness for many people, though cognitive therapy alone is far less effective than SSRI ther-

apy alone. Most people are able to reach a level of normal perspective about body image and return to full function within daily life.

See also [DEPRESSION](#); [EATING DISORDERS](#); GENERAL ANXIETY DISORDER (GAD); OBSESSIVE—COMPULSIVE DISORDER; PLASTIC SURGERY; [SOMATIZATION DISORDER](#).

brief reactive psychosis A trauma- or stress-induced psychotic episode (break with reality) that lasts longer than one day but less than one month. Symptoms may include HALLUCINATION, DELUSION, disordered speech, nonsensical expressions or thought processes, and strange or bizarre behavior such as outbursts of laughing without provocation or sitting motionless for hours and then returning to normal activities as though nothing out of the ordinary had happened. Often the episode is more apparent to others than to the person and may end before there is enough concern for family, friends, or co-workers to seek medical attention for the person. When symptoms result in a doctor's evaluation, treatment may be a combination of short-term ANTIPSYCHOTIC MEDICATIONS and PSYCHOTHERAPY to address the underlying trauma or stress. Treatment usually resolves the psychotic episode.

See also [ACUTE STRESS DISORDER](#); COGNITIVE FUNCTION AND DYSFUNCTION; STRESS AND STRESS MANAGEMENT.



cognitive therapy A therapy approach that helps a person recognize negative or unhelpful thought patterns and replace them with positive and helpful ones. Though there are different forms of cognitive therapy, the underlying foundation of cognitive therapy establishes thought as the basis for emotion and behavior. Conscious awareness of one's thoughts thus provides the ability to change one's emotions (feelings) and behaviors (actions).

Cognitive therapy is often effective treatment for DEPRESSION, GENERAL ANXIETY DISORDER (GAD), BIPOLAR DISORDER, and similar psychologic conditions. Cognitive therapy tends to produce results more rapidly (less than 20 visits with the therapist) than many other methods of therapy. This brevity is especially appealing to people who do not have the resources or time to undergo conventional PSYCHOTHERAPY, which often takes years before progress is apparent.

See also [BEHAVIOR MODIFICATION THERAPY](#); MIND—BODY INTERACTIONS.

conduct disorder A behavioral disorder in which a child engages in behaviors that disregard social norms and the rights of others. A child who has conduct disorder may frequently become involved in fights, be truant from school, be in trouble at school, bully others, shoplift, or run away from home. The diagnostic path includes a comprehensive medical examination to rule out physical causes for symptoms and may include evaluation for substance abuse. Treatment is often a combination of BEHAVIOR MODIFICATION THERAPY and COGNITIVE THERAPY for the child individually and sometimes also for the family. Appropriate intervention and treatment can turn the cycle of destructive behavior before it results in long-term consequences.

See also ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD); OPPOSITIONAL DEFIANT DISORDER.

conversion disorder The expression of emotional issues through physical symptoms that typically come on suddenly, often after a traumatic experience, and commonly involve some sort of debilitating loss of function such as inability to see or apparent PARALYSIS of an extremity. Older terminology for such losses includes hysterical blindness and hysterical paralysis.

The concern the person feels and expresses about the loss is disproportionately minor, and the doctor is unable to detect any physiologic or physical causes for the symptoms. Most often the episode of symptoms resolves on its own within a few weeks, as the precipitating emotional or psychologic concern improves or goes away. PSYCHOTHERAPY, COGNITIVE THERAPY, OR BEHAVIOR MODIFICATION THERAPY is often effective treatment. It is also important to provide appropriate care for the involved function, such as passive exercise for apparently paralyzed limbs to prevent the muscles from atrophying.

See also ACUTE STRESS DISORDER; BODY DYSMORPHIC DISORDER; BRIEF REACTIVE PSYCHOSIS; COPING MECHANISMS; EATING DISORDERS; FACTITIOUS DISORDERS; HYPOCHONDRIASIS; MIND—BODY INTERACTIONS; SOMATIZATION DISORDER; STRESS AND STRESS MANAGEMENT.

coping mechanisms The emotional and behavioral strategies people use to accommodate and recover from stressful circumstances in their lives over which they have little control. Numerous extrinsic and intrinsic factors shape and influence the coping mechanisms available to an individual. Among these factors are

- culture and generation
- financial or economic status
- personal experiences with crisis or disaster
- seriousness of the situation

Coping mechanisms, when they are positive, move a person toward regaining control over the situation and the ability to manage its circumstances. When they are negative, coping mechanisms often instead result in responses that perpetuate dysfunction or even the crisis itself. Because coping mechanisms are learned behaviors, it is possible for people to identify those that do not work well for them and replace them with others that are more successful.

See also [ANGER AND ANGER MANAGEMENT](#); [BEHAVIOR MODIFICATION THERAPY](#); [COGNITIVE THERAPY](#); [PSYCHOTHERAPY](#); [STRESS AND STRESS MANAGEMENT](#).

cyclothymic disorder Alternating, short-term periods (usually days) of elation and melancholy, milder than the cyclic periods of [MANIA](#) and [DEPRES-](#)

[SION](#) that define [BIPOLAR DISORDER](#). Other people commonly view the person as extremely moody or emotionally fragile though able to function reasonably well in work and social settings when at either mood extreme and quite well during periods of mood moderation. Some psychiatrists consider cyclothymic disorder, also called cyclothymia, to be a precursor (precondition) to bipolar disorder though other psychiatrists consider it a separate condition.

[COGNITIVE THERAPY](#) and [BEHAVIOR MODIFICATION THERAPY](#) are the most effective treatments, providing understanding of the disorder and teaching ways to accommodate the extremes of the mood swings so as to maintain appropriate interactions with others. Medications used to treat bipolar disorder may improve symptoms that disrupt the person's ability to function (such as job performance or fulfilling family responsibilities). Alternative and complementary approaches such as [BIOFEEDBACK](#) and [HYPNOSIS](#) may also improve the person's ability to cope with mood extremes.

See also [COPING MECHANISMS](#).

delusion A false perception or belief that persists even in confrontation with a reality that demonstrates its falseness. There may be an element of absurdity or bizarreness to the delusion or the delusion may appear to have some plausibility until closer examination refutes it. Many people have delusions yet function normally in the world. Delusions of persecution, being followed or watched, or infidelity in a relationship can result in behaviors that cause distress for the person and for others. There is no particular treatment for delusions. Delusions are also common components of psychotic disorders such as SCHIZOPHRENIA, in which case treatment attempts to manage symptoms of the disorder overall.

See also COGNITIVE FUNCTION AND DYSFUNCTION; HALLUCINATION; PARANOIA; PSYCHOSIS.

depression A psychologic condition of diminished emotional, cognitive, and physical function. Everyone feels sad and out of sorts with the events in their lives at some point. When these feelings interfere with the activities of daily life, they constitute clinical depression (also called major depression), a health condition that requires medical treatment. About 25 percent of adults and 12 percent of teens in the United States have depression, though fewer than half seek treatment.

Suicide is a significant risk in untreated depression. It is important to take seriously statements people make about taking their own lives or “ending it” and to do what is possible to help them get appropriate evaluation and care.

Symptoms and Diagnostic Path

The common symptoms of depression include

- feeling hopeless, worthless, helpless, or empty
- loss of interest in activities, work, friends, and family
- diminished LIBIDO (interest in sex), SEXUAL DYSFUNCTION, OR ERECTILE DYSFUNCTION
- difficulty concentrating and remembering
- sleep disturbances—sleeping all the time, being unable to sleep, or changes in the usual sleep pattern
- chronic HEADACHE, gastrointestinal distress, or body aches and discomforts that do not have apparent cause or respond to efforts to relieve them
- irritability, short temper, restlessness
- thoughts of death or ways to take one’s own life

The diagnostic path begins with a comprehensive physical examination, NEUROLOGIC EXAMINATION, and evaluation for substance abuse because numerous common health conditions (such as untreated HYPOTHYROIDISM or ANEMIA) and many drugs can cause symptoms of depression. Further evaluation includes psychologic assessment and an attempt to determine whether the person may be contemplating suicide.

Treatment Options and Outlook

About 80 percent of people who have depression take ANTIDEPRESSANT MEDICATIONS, some as sole treatment and others in combination with PSYCHOTHERAPY. The most commonly prescribed anti-

depressants are the selective serotonin reuptake inhibitors (SSRIs), which became available in the 1990s. Psychotherapy alone is sufficient treatment for some people who have mild symptoms. There are numerous types of psychotherapy, some of which are able to make rapid progress in improving symptoms and others that extend over months to years in an effort to fully expose, understand, and address the issues underlying the depression.

Alternative and complementary therapies that are often helpful include ACUPUNCTURE, MEDITATION and other stress relief measures, and mind-body approaches such as YOGA and TAI CHI. A number of studies show that one to two hours of physical exercise daily has the same effect as commonly prescribed antidepressant medications on reducing symptoms of mild to moderate depression. The herbal remedy St. JOHN'S WORT, available without a doctor's prescription as a dietary supplement in the United States, also may relieve symptoms of depression as effectively as prescription antidepressant medications. Many European countries regulate St. John's wort as a prescription product and doctors prescribe it as a first-line treatment for mild to moderate depression.

Do not take St. JOHN'S WORT when taking a prescription antidepressant. Doing so can result in a potentially life-threatening complication called serotonin syndrome.

ELECTROCONVULSIVE THERAPY (ECT), which uses electricity to momentarily disrupt the NERVE signals in the BRAIN, is an effective treatment for severe depression that does not improve with medications or for people who cannot take antidepressants.

Risk Factors and Preventive Measures

Family history is a significant factor for developing depression or related conditions such as CYCLOTHYMIC DISORDER, BIPOLAR DISORDER, and DYSTHYMIC DISORDER. Depression may also develop in reaction to persistent, intense stress or a traumatic event such as the death of a loved one or diagnosis with a serious physical illness such as CARDIOVASCULAR DISEASE (CVD) or cancer.

Hormonal shifts in menstruating women increase the risk for depression; women who have

substantial PREMENSTRUAL SYNDROME (PMS) symptoms also have a higher likelihood for developing depression. As well, nearly all women experience mild depressive symptoms in the first few weeks after childbirth and up to 20 percent develop full depression (POSTPARTUM DEPRESSION) that may last as long as a year.

Researchers also have identified proteins associated with depression that either are missing or are present in high levels. Early diagnosis and initiation of treatment are the most effective measures for heading off serious depression, though there are no measures to actually prevent depression from developing.

See also EXERCISE AND HEALTH RISK REDUCTION; GENERALIZED ANXIETY DISORDER (GAD); HORMONE; MENSTRUAL CYCLE; POST-TRAUMATIC STRESS DISORDER (PTSD); SUICIDAL IDEATION AND SUICIDE.

dissociative disorder A psychiatric disorder in which a person creates intentional though often not conscious separation between self and a traumatic event. The most common form of dissociative disorder is dissociative amnesia, a form of memory loss in which the person does not remember the circumstances of a trauma, such as childhood abuse or SEXUAL ASSAULT, and may not remember that the events occurred at all. Amnesia episodes are generally brief and contained to specific periods of time.

In dissociative fugue the amnesia is more extensive and the person may adopt a new identity and life, believing he or she is the created identity and dissociating entirely from the real identity and life. Dissociative fugue typically follows a significant trauma, such as living through a major natural disaster. The person may assume the created identity for months and sometimes years. Though dissociative fugue often appears as an attempt to walk away from difficulties or responsibilities, the person may not remember the fugue upon returning to his or her real identity.

The most extreme form of dissociative disorder is dissociative identity disorder (previously called multiple personality disorder) in which one person has two or more personalities. A person who has dissociative identity disorder typically experienced overwhelming trauma, such as abuse or the loss of a parent or other family members, in child-

hood at a time of vulnerability in personal development of sense of self. The various personalities may know of each other or be unaware that the others exist. Dissociative identity disorder is highly debilitating.

Treatment may combine ANTIPSYCHOTIC MEDICATIONS and intensive PSYCHOTHERAPY. The extent to which treatment succeeds depends on multiple factors, which are difficult to predict at the onset of treatment. RECURRENCE and relapse are common.

See also ACUTE STRESS DISORDER; BRIEF REACTIVE PSYCHOSIS.

dysthymic disorder Low-intensity, long-term or chronic DEPRESSION. A key characteristic of dysthymic disorder, also called dysthymia, is that the

person is generally able to function in the world though does not feel much joy or pleasure. Irritability, tiredness, and disinterest in most activities are other hallmark symptoms. Treatment that combines therapy (such as COGNITIVE THERAPY or BEHAVIORAL MODIFICATION THERAPY) and ANTIDEPRESSANT MEDICATIONS is often effective in diminishing symptoms and helping affected people learn productive COPING MECHANISMS to accommodate aspects of their lives that cause stress. Alternative and complementary methods such as BIOFEEDBACK, HYPNOSIS, MEDITATION, and VISUALIZATION are often helpful for reducing symptoms as well as restoring a sense of control about the person's life circumstances.

See also ST. JOHN'S WORT; STRESS AND STRESS MANAGEMENT.



eating disorders Psychologic conditions in which the person restricts food intake because of the belief that he or she is overweight. Eating disorders affect 10 times as many girls and women as boys and men. There are two main types of eating disorder: anorexia nervosa and bulimia nervosa.

Anorexia nervosa With anorexia nervosa, the person avoids eating, eats only very small amounts of certain foods, vomits after eating, or excessively uses laxatives and diuretics to reduce body weight. Some people who have anorexia nervosa also exercise compulsively and excessively to further drive down body weight. The person weighs herself numerous times each day, often following obsessive rituals (such as spitting or urinating before stepping on the scale, completely undressing, or taking off jewelry) to obtain the lowest weight possible. Even when weight reaches an unhealthy low, the person still believes she is overweight.

Bulimia nervosa In bulimia the person compulsively binges (eats excessive amounts of food in a short period of time), then compensates through inappropriate behaviors, such as induced vomiting or excessive laxative use, to eliminate the food. People who have bulimia often remain at normal weight or slightly below because they do consume calories during bingeing episodes, though believe they are excessively overweight.

Symptoms and Diagnostic Path

Because eating disorders incorporate secretive behaviors, symptoms may be subtle until weight loss (in anorexia particularly) is severe. Indications of an eating disorder include

- moving food around on the plate but not eating any of it

- self-proclaimed weight “problems” though excessively thin
- delayed or irregular MENSTRUATION
- going to the bathroom during or immediately after meals
- supplies of laxatives, diuretics, and enemas
- damaged tooth enamel (from vomiting)

The diagnostic path includes a comprehensive physical examination to detect signs of malnourishment or damage to the body resulting from prolonged inadequate nutrition. The KIDNEYS and HEART are most vulnerable to such damage.

Treatment Options and Outlook

The standard of care for treatment is a three-level approach:

- restoring body weight to a healthy range, which may require nutritional support or supplementation as well as supervised meals
- PSYCHOTHERAPY
- ANTIDEPRESSANT MEDICATIONS, usually selective serotonin reuptake inhibitors (SSRIs)

Treatment for anorexia is often a long-term process; treatment for bulimia tends to be more effective. Some people recover fully, though many deal with eating issues for most of their lives. SUDDEN CARDIAC DEATH remains a lifelong risk in people who have anorexia.

Risk Factors and Preventive Measures

Researchers do not know what causes eating disorders though believe they result from an interplay of genetic and environmental or psychosocial factors such as family relationships and self-

esteem issues. Though eating disorders are not preventable, early intervention and treatment can prevent further health conditions and minimize the damage to the body that severe food deprivation causes.

See also [BODY DYSMORPHIC DISORDER](#); [DEPRESSION](#); [DIET AND HEALTH](#); [NUTRITIONAL NEEDS](#); [OBESITY](#); [SOMATIZATION DISORDER](#); [STARVATION](#).

electroconvulsive therapy (ECT) A treatment for severe [DEPRESSION](#) that does not respond to treatment with [ANTIDEPRESSANT MEDICATIONS](#). ECT is also sometimes effective for severe [MANIA](#) or [BIPOLAR DISORDER](#) when either condition fails to improve with other treatments. ECT uses a mild electric shock to the outside of the skull to momentarily disrupt the electrical activity of the [BRAIN](#). The disruption causes the brain to release a flood of neurotransmitters, such as serotonin, [DOPAMINE](#), [EPINEPHRINE](#), and [NOREPINEPHRINE](#). These neurotransmitters, which are biochemical messengers that convey electrical impulses among the neurons ([NERVE](#) cells) in the brain, strongly affect mood and emotion. The typical course of treatment with ECT is up to 3 treatments per week for as many as four weeks (12 treatments total).

The psychiatrist performs ECT after the person receives general [ANESTHESIA](#), applying electrodes one on each side of the person's head. The actual discharge of electrical energy lasts about two seconds. Medications to relax the muscles and block their ability to receive messages from the brain during the treatment prevent the body from reacting to the seizures occurring in the brain. The person emerges from the anesthesia about 10 minutes after the shock and goes to the recovery room until fully awake. Some people experience short-term memory loss and brief cognitive dysfunction or disorganization of thoughts for a short time after the ECT.

See also [COGNITIVE FUNCTION AND DYSFUNCTION](#); [MEMORY AND MEMORY IMPAIRMENT](#); [NEURON](#); [NEUROTRANSMITTER](#).

factitious disorders Psychiatric conditions in which the person contrives the symptoms of an illness (physical or psychological). Despite the purposeful contrivance of symptoms, the person is unable to stop the behavior. The factitious disorder

may have symptoms that are primarily psychological, primarily physical (also called [Munchausen syndrome](#)), or a combination of psychological and physical. People who have factitious disorders often see multiple doctors in different clinics and hospitals and sometimes in different cities. Frequently they have undergone numerous invasive procedures and surgeries by the time doctors begin to realize a psychiatric condition is underlying. Characteristics of factitious disorders include

- persistent symptoms that are inconsistent with diagnostic findings
- symptoms that change after treatment begins
- eagerness to undergo invasive procedures and surgeries
- unwillingness to allow current health-care providers to consult with previous health-care providers
- reliable treatments fail to work in the expected ways

Diagnosis of factitious disorders is difficult because the person typically denies any element of contrivance about his or her health problems and symptoms despite confrontation with evidence such as test results. The concern is twofold: The person may do serious harm to himself or herself through the creation of symptoms or treatment for them, and the person extensively consumes expensive and often limited medical resources. Another person, such as a family member, who knows of the factitious disorder can sometimes mitigate the risks to the person's well-being by alerting health-care providers. However, overall, treatment for factitious disorders (and especially [Munchausen's syndrome](#)) is not very successful.

Factitious disorder by proxy, also called [Munchausen's syndrome by proxy](#), is a variant in which the person creates symptoms in another person, often under the guise of caring for the person, and then steps into the role of seeking medical attention for the person. [Munchausen's syndrome by proxy](#) most commonly involves a parent (usually mother) who creates symptoms in a child; less common manifestations include an adult child who creates symptoms in a parent or a

spouse who creates symptoms in the other spouse. In Munchausen's syndrome by proxy, which may have legal consequences, protection of the other person is of utmost importance.

See also CHILD ABUSE; DOMESTIC VIOLENCE; ELDER ABUSE; SOMATIZATION DISORDERS.

generalized anxiety disorder (GAD) A psychologic condition in which the person experiences exaggerated worry and anxiety that generates physical symptoms such as excessive sweating, trembling, and tics or MUSCLE twitches. Gastrointestinal symptoms, such as NAUSEA and DIARRHEA, are also common. Symptoms may be episodic (come and go) or persistent (always present) and often interfere with, though do not prevent, the person's function in the world. People who have GAD commonly have other psychologic conditions as well, such as DEPRESSION, OBSESSIVE-COMPULSIVE DISORDER (OCD), POST-TRAUMATIC STRESS DISORDER (PTSD), PANIC DISORDER, or PHOBIA.

After medical and NEUROLOGIC EXAMINATION to rule out organic or neurologic causes for symptoms, the doctor is likely to recommend treatment that combines PSYCHOTHERAPY and ANTIANXIETY MEDICATIONS. Some people also benefit from ANTIDEPRESSANT MEDICATIONS (notably selective serotonin reuptake inhibitors; SSRIs), which further reduce agitation and provide a more balanced emotional landscape. For some people GAD is a limited condition that, once successfully treated, does not return. For many people, however, GAD is a chronic or recurrent condition that periodically requires treatment. Researchers do not know what causes GAD, and there are no measures to prevent its development.

See also ORGANIC BRAIN SYNDROME; PARKINSON'S DISEASE.

hallucination A false sensory perception such as hearing voices or seeing objects that are not there. Hallucinations may affect any or a combination of the five senses—vision, hearing, taste, touch, and smell. Hallucinations may occur in numerous psy-

chiatric conditions as well as neurologic conditions such as ALZHEIMER'S DISEASE and PARKINSON'S DISEASE. They may also occur as undesired side effects of numerous medications and sometimes with high FEVER. A hallucination is entirely real to the person experiencing it. When the cause of persistent hallucination is not clear, the doctor may undertake comprehensive NEUROLOGIC EXAMINATION and psychiatric examination.

See also COGNITIVE FUNCTION AND DYSFUNCTION; DELUSION.

hypochondriasis Obsessive fear that something is wrong with one's physical health. Though it is normal to worry about health, even inappropriately or excessively at times, the person who has hypochondriasis is inordinately preoccupied with observations of natural body functions that he or she perceives as indications of illness. This worry may be so overwhelming as to periodically prevent the person from engaging in normal activities. The person frequently sees health-care providers to evaluate these perceived symptoms. COGNITIVE THERAPY and BEHAVIOR MODIFICATION THERAPY are often successful in helping people recognize and understand the dysfunctional nature of their health worries and learn ways to manage their worry and anxiety. HYPNOSIS is also sometimes helpful.

See also BODY DYSMORPHIC DISORDER; CONVERSION DISORDER; FACTITIOUS DISORDERS; SOMATIZATION DISORDER; STRESS AND STRESS MANAGEMENT.

insanity A legal term within the practice of medicine that identifies the circumstance in which a person is cognitively or emotionally unable to make decisions and manage his or her affairs, including matters related to health care. In matters of law, a clinical diagnosis of insanity generally means a person was unaware of the difference between right and wrong at the time of a specific action, though in the United States this varies among states. Insanity is not a clinical diagnosis.

See also NERVOUS BREAKDOWN.

mania A psychotic disorder of extremely elevated mood. A person who has mania, also called manic disorder, may appear euphoric and energetic almost to a level of hyperactivity though also is characteristically irritable and impatient. The person often cannot sleep and expresses jumbled, sometimes irrational thoughts and ideas. Mania distorts a person's judgment and can result in inappropriate behaviors such as uncontrolled spending or sexual indiscretions. The diagnostic path includes comprehensive medical examination including BLOOD tests to check for conditions such as HYPERTHYROIDISM (overactive THYROID GLAND) or other endocrine disturbances that could account for symptoms. Medications to treat mania include

- the antiseizure medications valproic acid (valproate), gabapentin, carbamazepine, and topiramate
- the ANTIPSYCHOTIC MEDICATIONS olanzapine, ziprasidone, quetiapine, clozapine, and risperidone
- the mood stabilizer lithium

With treatment the symptoms of mania are manageable and most people are able to return to functional, productive lifestyles. Failure to continue taking medications, a common concern, can result in a return of symptoms.

See also [BIPOLAR DISORDER](#); [DEPRESSION](#); [PSYCHOSIS](#).

multiple personality disorder See [DISSOCIATIVE DISORDER](#).

Munchausen syndrome See [FACTITIOUS DISORDERS](#).

nervous breakdown A casual term for an acute psychiatric condition that suddenly manifests symptoms in a person who had otherwise appeared normal and functional. The underlying premise of a nervous breakdown is that the person reaches his or her breaking point as a consequence of accumulated mental stress or of a single, traumatic precipitating event, such as the death of a loved one. The term *nervous breakdown* came into vogue in the early decades of the 20th century as an attempt to attribute physical causes to mental illnesses. Common usage broadly applied the term to numerous conditions though typically referred to those from which the person eventually recovered.

See also [ACUTE STRESS DISORDER](#); [BIPOLAR DISORDER](#); [BRIEF REACTIVE PSYCHOSIS](#); [DEPRESSION](#); [GENERALIZED ANXIETY DISORDER \(GAD\)](#); [POST-TRAUMATIC STRESS DISORDER](#); [SCHIZOPHRENIA](#).

neurosis A pattern of thought or behavior that causes disruption in a person's life but does not prevent the person from functioning in daily activities and does not represent a break from reality. Nearly everyone has some neuroses, which commonly arise from ineffective COPING MECHANISMS. Neurotic behaviors may include minor compulsive acts (such as starting a set of stairs with the same foot first or sitting in a particular row of seats at the movie theater), excessive worrying, or irrationally avoiding certain circumstances (such as elevators because of fear of getting stuck). Most mental health professionals do not consider neurosis a mental illness.

See also [OBSESSIVE-COMPULSIVE DISORDER \(OCD\)](#); [PHOBIA](#); [PSYCHOSIS](#).

obsessive-compulsive disorder (OCD) A psychiatric disorder in which the person engages in ritualistic, often repetitive behaviors to an extent that interferes with, and may prevent, normal function in everyday activities. OCD is a type of anxiety disorder in which unreasonable worry crafts the ritualistic behaviors, which are dysfunctional methods for accommodating the worry. For example, washing the hands seven times each after going to the bathroom may be an accommodation for an unrealistic worry about, or fear of, infectious disease. Walking three times up and down the sidewalk before entering the house when returning from work may be an accommodation for the unfounded fear of an intruder being in the house or to affirm the presence of someone who is supposed to be there.

The person generally has no conscious desire to engage in the behaviors and may instead consciously desire not to engage in them but is unable to stop. This desire may become so intense as to cause the person to avoid circumstances that activate the behavior—for example, not using public bathrooms to avoid hand washing rituals or entering the home from the garage or back door to avoid entry rituals. OCD begins in childhood for many people and often progresses in adulthood. Other psychologic conditions, such as [DEPRESSION](#) and [PANIC DISORDER](#), are also common in people who have OCD.

[ANTI-ANXIETY MEDICATIONS](#) and [ANTIDEPRESSANT MEDICATIONS](#), notably selective serotonin reuptake inhibitors (SSRIs) and tricyclics, are often effective in relieving symptoms. The tricyclic antidepressants clomipramine and imipramine are especially effective. [BEHAVIORAL MODIFICATION THERAPY](#) and [COGNITIVE THERAPY](#) help the person gain control over his or her thoughts and actions regarding compulsive behaviors. OCD, like other psychologic

conditions, likely has genetic as well as environmental foundations. For many people OCD is a chronic condition that requires lifelong treatment, though treatment successfully manages symptoms to allow normal participation in daily life, work situations, and social interactions.

See also [GENERALIZED ANXIETY DISORDER \(GAD\)](#); [NEUROSIS](#); [PSYCHOSIS](#).

oppositional defiant disorder A behavior disorder in which a child expresses open defiance and constant challenge toward parents, teachers, and other adult authority figures. The behaviors appear intended to create irritation and annoyance and consist of

- persistent arguing with adults
- questioning or refusing to follow rules
- deliberately hurtful comments
- perpetually angry demeanor

The expression of defiant behaviors commonly occurs during two periods: around age three and at [ADOLESCENCE](#). Some researchers believe oppositional defiant disorder reflects difficulty the child experiences in the attempt to separate from parents or primary caregivers to establish his or her independent identity.

The diagnostic path begins with a comprehensive medical examination to rule out physical causes for symptoms and may include evaluation for substance abuse. Treatment is often a combination of [BEHAVIOR MODIFICATION THERAPY](#) and [COGNITIVE THERAPY](#) for the child individually and sometimes for the whole family. Most children respond to treatment.

See also [ATTENTION DEFICIT HYPERACTIVITY DISORDER \(ADHD\)](#); [CONDUCT DISORDER](#).

panic disorder A psychologic condition in which a person feels extreme fear or panic without provocation (unlike **PHOBIA**, which triggers fear only when facing confrontation with the focus of the phobia). Such panic attacks are the hallmark symptoms of panic disorder and often occur without warning. Symptoms of panic attack can be severe enough to mimic **HEART ATTACK** and include

- racing **HEART RATE** (pulse) and rapid **BREATHING** or difficulty breathing
- profuse sweating or cold sweat
- **CHEST PAIN**
- **HEADACHE**
- tingling in the toes and fingers

The diagnostic path begins with a prompt assessment to rule out cardiovascular causes (such as **MITRAL VALVE PROLAPSE**, heart attack, or **STROKE**) for the symptoms. The most effective treatment for panic disorder is a combination of **BEHAVIOR MODIFICATION THERAPY** and **COGNITIVE THERAPY**. Relaxation and stress management techniques, **HYPNOSIS**, and sometimes **BIOFEEDBACK** can help the person cope with panic attacks when they occur. Some people further benefit from short-term treatment with **ANTI-ANXIETY MEDICATIONS**. With treatment many people are able to overcome panic disorder.

See also **ACUTE STRESS DISORDER**; **GENERALIZED ANXIETY DISORDER (GAD)**; **STRESS AND STRESS MANAGEMENT**.

paranoia A person's unfounded and often disabling suspicion or fear that others are watching, following, or in some other fashion persecuting the person. Paranoia is most commonly a component of psychotic disorders such as **SCHIZOPHRENIA**

though may occur in milder form as a **DELUSION** (sometimes called delusional disorder when it persists). Often it is a family member who brings the person for treatment because the person's expressions or behaviors turn violent.

Paranoia is difficult to treat because the person's suspicion prevents him or her from seeking care or trusting doctors. **ANTI-PSYCHOTIC MEDICATIONS** and **PSYCHOTHERAPY** may reduce the intensity of the paranoia, particularly when other psychiatric issues are under control. Paranoia may also be a symptom of degenerative neurologic disorders such as **ALZHEIMER'S DISEASE**, **ORGANIC BRAIN SYNDROME**, and **BRAIN** damage due to **TRAUMATIC BRAIN INJURY (TBI)** or **STROKE**.

See also **COGNITIVE FUNCTION AND DYSFUNCTION**; **HALLUCINATION**; **PSYCHOSIS**; **VIOLENCE**.

pervasive developmental disorders (PDD) See **AUTISM**.

phobia An intense, irrational fear that prevents the person from normal function and interaction. A phobia such as **agoraphobia** (fear of public places) or **social phobia** (fear of being in groups of people) may keep the person from participating in activities vital to the ability to function in the world. Other phobias are specific and are easier to avoid, such as **arachnophobia** (fear of spiders) or **pyrophobia** (fear of fire). **BEHAVIOR MODIFICATION THERAPY**, which teaches behavior methods for overcoming the phobia, and **COGNITIVE THERAPY**, which teaches understanding of the thinking patterns that result in phobias, often succeed in managing long-term phobic symptoms. Gradual, controlled exposures to the circumstance that causes the fear effectively cures the phobia for many people.

COMMON PHOBIAS

acrophobia	fear of heights
agoraphobia	fear of open spaces or crowded public places
altophobia	fear of heights
aviophobia	fear of flying
claustrophobia	fear of enclosed spaces
herpetophobia	fear of snakes
hydrophobia	fear of water
pyrophobia	fear of fire
sociophobia	fear of being in social gatherings and events
technophobia	fear of technology
xenophobia	fear of strangers

See also OBSESSIVE–COMPULSIVE DISORDER (OCD).

postpartum depression A depressive disorder that occurs after **CHILDBIRTH**. Postpartum depression may affect as many as 20 percent of women who have recently given birth. Although postpartum depression is more likely to occur in subsequent pregnancies if the woman experienced it after one **PREGNANCY**, it can develop in women who had previous pregnancies without postpartum depression. It is common for women to feel somewhat sad after giving birth, but these feelings generally pass within a few weeks, and doctors believe they result from the hormonal shifts taking place in the woman’s body.

Postpartum depression occurs when the feelings deepen into sensations of hopelessness, being overwhelmed, extreme mood swings, or being inadequate as a mother. Postpartum depression, like other depressive disorders, is a serious clinical condition that requires medical evaluation and treatment. The most effective treatment is **PSYCHOTHERAPY** in combination with **ANTIDEPRESSANT MEDICATIONS**. Most women recover within six months to a year, though in some women the depressive disorder becomes chronic and requires ongoing treatment.

A rare complication of postpartum depression is postpartum **PSYCHOSIS**, in which the woman experiences a complete break with reality and requires intense care, usually in an inpatient setting. Doctors treat postpartum psychosis as any other psychosis, with **ANTIPSYCHOTIC MEDICATIONS** and psychotherapy. Postpartum psychosis is very

severe and likely to return if the woman has another pregnancy.

See also **PARENTING**; **POST-TRAUMATIC STRESS DISORDER (PTSD)**; **STRESS AND STRESS MANAGEMENT**.

post-traumatic stress disorder (PTSD) A delayed-onset anxiety disorder that develops months to years after a traumatic experience or event. The event may be personal, such as **SEXUAL ASSAULT** or **CHILD ABUSE**, or a widespread disaster such as surviving a plane crash or tornado. Though the first awareness of PTSD symptoms came from soldiers returning from war with “battle fatigue,” PTSD can affect anyone who has had a traumatic experience; more than five million Americans have PTSD.

Symptoms and Diagnostic Path

Ordinary events and experiences not obviously related to the trauma may trigger symptoms, and symptoms often worsen at the anniversary of the experience or event. Common symptoms of PTSD include

- flashbacks and nightmares of the traumatic event
- a sense of emotional numbness or distance
- panic-like reactions to places, people, and circumstances that evoke memories of the trauma
- feelings of guilt or unworthiness about surviving when others died

The diagnostic path includes a medical examination to rule out physical causes for symptoms as well as comprehensive psychologic evaluation to distinguish PTSD from other psychologic disorders.

Treatment Options and Outlook

The most effective treatment approach is a combination of **PSYCHOTHERAPY** and **ANTI-ANXIETY MEDICATIONS** OR **ANTIDEPRESSANT MEDICATIONS**. The process of uncovering the event or experience is sometimes extensive, particularly in the case of childhood abuse or trauma. Sometimes the person has a diagnosis of **GENERAL ANXIETY DISORDER (GAD)** OR **DEPRESSION** then discovers through therapy the underlying trauma. Treatment helps many people

who have PTSD understand the source of their symptoms and accept the circumstances of what happened to them, though for others the trauma is too great and symptoms are difficult to manage.

Risk Factors and Preventive Measures

Anyone who experiences a traumatic event may develop PTSD. There are no measures to identify who is particularly susceptible or to prevent PTSD. Early detection and initiation of treatment help minimize the extent to which PTSD causes disruption in the person's life.

See also [ACUTE STRESS DISORDER](#); [BRIEF REACTIVE PSYCHOSIS](#).

psychosis Any of numerous psychiatric disorders in which there is a complete break with reality. A person who has a psychotic disorder commonly experiences [DELUSION](#) (untrue belief) and [HALLUCINATION](#) (untrue sensory perception) and exhibits bizarre behavior in response. [SCHIZOPHRENIA](#), [MANIA](#), [BIPOLAR DISORDER](#), [DISSOCIATIVE DISORDER](#), [OBSESSIVE–COMPULSIVE DISORDER \(OCD\)](#), and personality disorders are among the more common psychoses. Often, components of multiple psychotic disorders coexist—that is, a person may have some symptoms of a dissociative disorder, some symptoms of OCD, and some symptoms of a personality disorder.

The diagnostic path is often complex and generally begins with a comprehensive [NEUROLOGIC EXAMINATION](#) to rule out organic causes (such as [ALZHEIMER'S DISEASE](#) or [BRAIN TUMOR](#)) that could

cause the symptoms. Substance abuse and long-term [ALCOHOLISM](#) may also cause psychosis. Psychotic disorders require treatment with medications, often multiple medications in various combinations that attempt to manage the range of symptoms. [PSYCHOTHERAPY](#) in combination with medications is sometimes more effective, though this depends on the psychotic behaviors. Severe psychotic disorders require intensive treatment in an inpatient hospital setting. Psychotic disorders are often chronic and difficult to treat, though understanding of brain biochemistry continues to evolve and result in new types of medications.

See also [ANTIANSIETY MEDICATIONS](#); [ANTIDEPRESSANT MEDICATIONS](#); [ANTIPSYCHOTIC MEDICATIONS](#); [NEUROSIS](#); [PARANOIA](#).

psychotherapy A collective term for the dozens of treatment approaches based on interaction and dialogue between a person and a mental health professional (therapist, psychologist, psychiatrist). Pure psychotherapy does not involve the use of medications; however, many people who are in psychotherapy also take medications to mitigate the symptoms of their conditions. Because many psychiatric disorders and psychologic conditions involve deeply rooted and complex issues, psychotherapy tends to extend over months to years. Some therapies specifically target narrow issues for rapid results, such as [BEHAVIOR MODIFICATION THERAPY](#) and [COGNITIVE THERAPY](#). The success of psychotherapy depends on many factors.

See also [ELECTROCONVULSIVE THERAPY \(ECT\)](#).

S-T

seasonal affective disorder (SAD) DEPRESSION that develops during the winter months when the hours of darkness exceed the hours of daylight. Researchers believe a key factor in SAD is an increase in the amount of MELATONIN the PITUITARY GLAND produces. Melatonin is a HORMONE that regulates the body's circadian cycle (wake and sleep pattern). Darkness stimulates melatonin release. Higher than normal levels of melatonin cause tiredness and reduce energy. Bright light causes the pituitary gland to back off melatonin production, causing wakefulness and alertness. Another factor may be the level of serotonin, a NEUROTRANSMITTER associated with mood, in the BRAIN.

Symptoms of SAD commonly appear each year during the winter months and include

- profound lethargy
- disinterest in life
- tiredness or urge to sleep
- craving for sweets (simple carbohydrates)
- weight gain

The most effective treatment for SAD is exposure to bright light, ideally sunlight outdoors. Walking an hour a day in the winter often dramatically improves symptoms, likely a combination effect of the exposure to light and exercise. Arranging one's workspace to have as much natural light as possible (or using light bulbs that emulate daylight) is often helpful for people who cannot get outdoors during daylight hours. Symptoms cause significant enough dysfunction in some people to warrant therapy with ANTIDEPRESSANT MEDICATIONS, typically selective serotonin reuptake inhibitors (SSRIs) to increase serotonin levels in the brain.

See also EXERCISE AND HEALTH RISK REDUCTION; POSTPARTUM DEPRESSION; [SLEEP DISORDERS](#); WALKING FOR FITNESS; WEIGHT LOSS AND WEIGHT MANAGEMENT.

schizophrenia A serious psychotic disorder with marked emotional, cognitive, and physical symptoms. Schizophrenia represents a profound and disabling break from reality. Researchers do not know what causes schizophrenia, though it tends to run in families, which suggests a genetic foundation is likely. Differences in BRAIN structure in people who have schizophrenia, apparent with diagnostic imaging, also suggest organic factors that likely affect the ways the brain receives, organizes, and processes information. Symptoms in men often begin in late ADOLESCENCE or early adulthood; symptoms in women tend to develop in early to middle adulthood. More than three million Americans have schizophrenia.

Symptoms and Diagnostic Path

There are five types of schizophrenia—catatonic, disorganized, paranoid, undifferentiated, and residual—that share many common symptoms as well as have unique symptoms. These symptoms must be continuous six months or longer and represent a dramatic and observable deterioration in function. Symptoms common to all types of schizophrenia, though present to differing degrees in different types, include

- DELUSION (untrue belief)
- HALLUCINATION (false sensory perception)
- chaotic or disordered thought processes and expression of ideas
- bizarre behavior and involuntary movement

- lack of emotional response or demeanor (flat affect)

The diagnostic path often includes COMPUTED TOMOGRAPHY (CT) SCAN OR MAGNETIC RESONANCE IMAGING (MRI) of the head to rule out physical causes, such as BRAIN TUMOR, for symptoms. Diagnosis is sometimes difficult because symptoms are similar to those of other psychotic disorders. There are no conclusive diagnostic procedures, and psychiatrists sometimes differ in their clinical opinions as to whether a person has schizophrenia or another psychotic disorder. However, treatment approaches are usually the same, at least initially.

Treatment Options and Outlook

Schizophrenia requires treatment with ANTIPSYCHOTIC MEDICATIONS to moderate and mitigate symptoms. Though these medications have significant side effects, they often restore the ability to interact in the world. Most people require several medications to adequately cover all symptoms. The balance of medication, both DRUG and dosage, is often a trial-and-error process as each person responds in a unique way to a particular medication as well as to combinations of medications. However, many people who have schizophrenia are able to work and engage in personal and social relationships once medications control their symptoms.

People who have schizophrenia are at increased risk for suicide, a risk that is most significant when treatment moderates symptoms and the person begins to reengage with normal life. It is common for DEPRESSION to emerge at this time. Psychiatrists often incorporate ANTIDEPRESSANT MEDICATIONS into the treatment regimen to offset this development.

Schizophrenia is a chronic disorder that requires lifelong, consistent treatment. Though it is essential for the person to continue medications as prescribed, many people fail to do so for various reasons. Some medications to treat schizophrenia are expensive, and all have potentially significant side effects that can make them unpleasant to take. Inherent in most forms of schizophrenia is distrust of others, a characteristic particularly prominent in paranoid schizophrenia. This distrust may combine with PARANOIA to cause the person to believe the medications are poisonous and refuse

to take them. Further supporting this distrust is the sometimes necessary step of involuntary hospitalization to treat severe symptoms, notably when the person becomes a threat to self or others. Inconsistency in complying with medication regimens results in relapses of symptoms.

Risk Factors and Preventive Measures

The only known risk factor for schizophrenia is family history, though researchers do not know the basis of the genetic connections. Most people who have schizophrenia have no known family history of the disorder. There are no measures to prevent schizophrenia.

See also [DISSOCIATIVE DISORDER](#); [NEUROSIS](#); [PERSONALITY DISORDER](#); [PSYCHOSIS](#).

sleep disorders Disturbances of normal sleep patterns. Though there are dozens of types of sleep disorders, they fall into three general categories: insufficient sleep, disrupted sleep, and excessive or inappropriate sleep.

The body requires adequate sleep to restore cellular functions throughout the body. The BRAIN is active on different levels during sleep than when awake. Dreaming is particularly important for restful sleep. Though the amount of sleep needed varies among individuals as well as with age, everyone needs a consistent amount and quality of sleep most nights of the week.

Sleep disturbances, and in particular sleep deprivation, most significantly affect the NERVOUS SYSTEM, altering cognitive function and memory as well as motor function, balance, spatial orientation, and coordination. Public health experts estimate that sleep deprivation causes more MOTOR VEHICLE ACCIDENTS than intoxication and more work-related injuries than any other single cause. Sleepy drivers are often unaware of the extent to which their drowsiness impairs judgment and reaction time. More than 40 million Americans have chronic sleep disorders.

Symptoms and Diagnostic Path

The symptoms of inadequate sleep include

- daytime tiredness
- inability to concentrate or remember simple directions

- irresistible urge to nap
- drowsiness when driving or engaged in repetitious activity
- excessive snoring (OBSTRUCTIVE SLEEP APNEA) or moving around (RESTLESS LEGS SYNDROME)

The diagnostic path begins with a comprehensive medical examination to rule out physical causes or health conditions, particularly obstructive sleep apnea. Evaluation in a sleep lab allows observation of sleep patterns (polysomnography study). The person may spend one to five nights in the sleep lab, depending on the suspected causes of sleep disturbances, during which technicians observe, videotape, and record vital information such as HEART RATE, BLOOD PRESSURE, and electrical activity in the brain. ELECTROENCEPHALOGRAPH (EEG) while awake and while asleep can detect subclinical SEIZURE DISORDERS or other abnormalities of the brain's electrical activity that may interfere with sleep.

Treatment Options and Outlook

Lifestyle measures are often successful in improving the amount and quality of restful sleep. One of the most important is going to bed at the same time every night, which helps the body establish a conscious rhythm of slowing down as that time approaches. Other lifestyle approaches to improve sleep include

- avoiding heavy meals, CAFFEINE, ALCOHOL, and tobacco within four hours of bedtime
- establishing quiet and darkness in the bedroom, even if a daytime sleeper because of night shift work
- getting 20 to 30 minutes of physical exercise, preferably outdoors, every day

Over-the-counter sleep aids often contain ANTI-HISTAMINE MEDICATIONS, which induce sleep. Prescription sleep aids are often sedatives. Though sleep aids are effective for occasional use, over the long term they are more likely to interfere with sleep than improve its quality. Most medications that induce sleep affect neuroreceptors in the brain, which alters the way the brain functions during sleep. The sleep aid may induce sleep but

prevent REM sleep and the dreams that occur during it, reducing the restful quality of the sleep.

MELATONIN supplementation can sometimes help readjust the body's rhythms to encourage sleep during daylight hours, particularly for night shift workers. Melatonin is a HORMONE the PITUITARY GLAND produces on a cyclic basis that initiates sensations of drowsiness when it is time to sleep. Warm chamomile tea, warm baths, or reading for 10 to 20 minutes before going to bed also may help the transition from the activities of the day to the calm that precedes restful sleep. Self-HYPNOSIS, relaxation techniques or audiotapes, and BIOFEEDBACK are other methods to prepare for sleep.

TO NAP OR NOT TO NAP

For many people who do not get enough sleep, the urge to nap during the day is irresistible. Though napping often provides a boost of energy and alertness in the short term, in the long term it can contribute to sleep disturbances such as insomnia.

Risk Factors and Preventive Measures

People who work night shifts and sleep during the day, which is counter to the body's natural circadian rhythm (cycle of sleep and wake), are most likely to have sleep disorders. Sleep disorders may result from physical conditions, such as obstructive sleep apnea or CHRONIC PAIN, as well as from neurologic disorders that affect BREATHING or MUSCLE control. OBESITY is the primary cause of obstructive sleep apnea. Sleep disturbances are common in many chronic health conditions, both physical and psychologic. These factors are often difficult for people to change. Other factors that influence sleep are alcohol and tobacco use, EATING HABITS and exercise patterns, and external environment (quiet or noisy, bright or dark). These are factors people can usually alter to improve the potential for sleep, once they become aware of the effects on sleep.

See also NARCOLEPSY.

somatization disorder Chronic perception of multiple illnesses and ailments for which doctors can find no clinical evidence. Stress often exacerbates symptoms. Because the physical complaints could indicate potentially serious illness, the most

common health-care response is to subject the person to comprehensive diagnostic testing. However, test results persistently produce no apparent physiologic cause for the symptoms. The person may go from one doctor to another, seeking diagnosis and treatment for symptoms that are all too real to the person regardless of the findings of diagnostic tests, causing the person to remain convinced he or she is seriously ill.

**CHRONIC PHYSICAL SYMPTOMS COMMON
IN SOMATIZATION DISORDER**

abdominal pain and bloating	BACK PAIN
CHEST PAIN	DIARRHEA
difficulty BREATHING (DYSPNEA)	dizziness
DYSMENORRHEA	ERECTILE DYSFUNCTION
HEADACHE	JOINT PAIN
MUSCLE weakness	NAUSEA
PALPITATIONS	SEXUAL DYSFUNCTION
swallowing difficulty	VOMITING

Researchers do not fully understand what causes somatization disorder, though some of its mechanisms are clear and occur in other psychiatric conditions such as BODY DYSMORPHIC DISORDER and GENERALIZED ANXIETY DISORDER (GAD). Some doctors may perceive the person is making himself or herself sick (FACTITIOUS DISORDERS). Recent research is uncovering new information about the integration among immune functions, neurologic functions, and psychologic functions (the field of PSYCHONEUROIMMUNOLOGY) that may reveal how these body systems affect the functions of each other in ways that shed light on conditions such as somatization disorder.

Diagnosis of somatization disorder is often difficult because the symptoms are real (the person experiences them, even though there are no apparent causes) and because many people see multiple doctors in their searches for answers. Consistent care from the same health-care provider is the most effective means for detecting and diagnosing somatization disorder.

Though psychiatric treatment or counseling could help many people understand the psychologic and emotional components to their symptoms, another function of the disorder is the flat refusal to acknowledge these components are present. In many situations the person may experience

side effects or complications as a result of invasive diagnostic procedures and even surgeries. Noninvasive treatments such as BIOFEEDBACK, ACUPUNCTURE, and VISUALIZATION are often helpful for people who have somatization disorder just as they are for people who have similar symptoms with identifiable physiologic causes. People who can gain insight into the health relationship between body and mind and who can use these body-mind methods are often able to satisfactorily control their symptoms for long-term relief.

See also CHRONIC FATIGUE SYNDROME; [CONVERSION DISORDER](#); FIBROMYALGIA; HYPOCHONDRIASIS; MIND-BODY INTERACTIONS; STRESS AND STRESS MANAGEMENT.

suicidal ideation and suicide Thoughts of killing oneself, attempting to kill oneself, or succeeding in killing oneself. The risk for suicide is highest among people who have DISSOCIATIVE DISORDER, clinical DEPRESSION (major depression), SCHIZOPHRENIA, and BIPOLAR DISORDER. Substance abuse and ALCOHOLISM are also risk factors. Stressful life events and circumstances heighten the risk and may serve as precipitating factors. People who have degenerative or debilitating physical health conditions may also contemplate or attempt suicide.

It is important to take seriously any comments a person makes about taking his or her life, and to encourage the person to seek help. Most communities have suicide hot lines or crisis intervention services.

Suicide is intensely traumatic and very difficult to understand for family members and friends. Though occasional thoughts of suicide are common and most people who talk about death or suicide make no attempts to take their own lives, many people who carry through with suicide give some indications (though sometimes subtle) that suicide is at least in their thoughts. Suicide among men is more likely to involve firearms or hanging; suicide among women is more likely to result from medication OVERDOSE. Loved ones often feel responsible and guilty for missing the clues.

A common misunderstanding about suicide is that discussing it encourages it. In most situations,

the reverse is more true. Many people are relieved to be able to discuss their fears and worries and are receptive to less drastic solutions that perhaps previously had not occurred to them. All states in the United States provide for involuntary hospitalization of people who present clear danger to themselves, though most have stringent criteria for determining whether such hospitalization is appropriate. Other preventive measures include appropriate treatment for the underlying psychologic condition or psychiatric disorder and close supervision or monitoring.

See also [END OF LIFE CONCERNS](#); [STRESS AND STRESS MANAGEMENT](#).

trichotillomania Compulsively pulling out one's HAIR such that hair loss occurs and is obvious. Pulling the hair results in a sense of relief from stress or anxiety. Trichotillomania often begins in early ADOLESCENCE and is more common in girls. There is commonly a precipitating event that is stressful or traumatic, though some research suggests the fluctuating hormonal environment within the body during PUBERTY may trigger the

condition. Some psychiatrists believe trichotillomania is a form of [OBSESSIVE–COMPULSIVE DISORDER \(OCD\)](#) because many people who have trichotillomania also engage in some degree of compulsive behavior such as counting rituals or repetitiously washing the hands. As well, the current therapeutic approach for trichotillomania is treatment with a combination of [BEHAVIOR MODIFICATION THERAPY](#) and medications such selective serotonin reuptake inhibitors (SSRIs) and the antiseizure medication valproate. These are the same medications used to treat OCD. People who are successful in changing their behavior often experience long-term relief, although the trichotillomania may return in times of intense stress.

COMMON MEDICATIONS TO TREAT TRICHOTILLOMANIA

clomipramine	fluoxetine
lithium carbonate	paroxetine
sertraline	valproate

See also [ALOPECIA](#); [ANTIDEPRESSANT MEDICATIONS](#); [DEPRESSION](#); [GENERALIZED ANXIETY DISORDER \(GAD\)](#); [STRESS AND STRESS MANAGEMENT](#).

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